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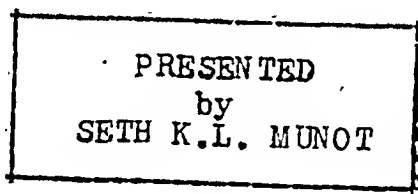
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Original Articles

RESULT OF THE FORECAST OF CHOLERA, SMALLPOX AND PLAGUE IN INDIA IN 1932 AND FORECAST FOR 1933*

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THE analysis of the results of my forecast of the incidence of cholera, smallpox and plague in 1932, recorded below, shows it to have been the most accurate of the three yet issued, in spite of the well-distributed rains of 1931 having made a forecast difficult. As the two previous forecasts also proved more correct than I had dared to hope, it now appears to be evident that my three years' very laborious studies of the incidence of these epidemic diseases in relation to the climatic conditions in India during the last sixty years have provided data from which moderately-accurate and practically-useful forecasts can be made several months ahead of the incidence of these three diseases. These forecasts are necessarily delayed and are less complete and up-to-date than they would be if they were worked out in India, instead of in London after the data have been received from India.

Result of cholera forecast for 1932

General Forecast.—'Not likely to exceed the average and will probably be well below it'.

Result.—Judging from the weekly figures nearly to the end of September 1932, and allowing for the average defect of the weekly returns below the final figures for each province during the three previous years, the total cholera deaths in India in 1932 do not appear likely much to exceed 100,000, unless Bengal, Assam and Madras show a considerable excess during the last quarter of the year. This rough estimate is about one-half the usual average for India, which would make the cholera rate in 1932 about the lowest since 1923. My forecast has thus proved correct, for all the provinces of India proper were much below the average except Bengal and Assam with approximately average cholera death rates up to September 1932. The detailed forecasts for the different areas may be recorded briefly as follows:—

Assam.—*Forecast*—low cholera in last four years, no epidemic likely, but some increase probable.

Result—slight increase in October 1931 to September 1932 on two former similar seasons.

Bengal.—*Forecast*—same as for Assam.

Result—not epidemic but slight increase on previous October to September rate.

Bihar and Orissa.—*Forecast*—average to low incidence.

Result—about average in Orissa and low in Bihar.

United Provinces.—*Forecast*—average to low.

Result—very low incidence.

Punjab.—*Forecast*—about the average.

Result—about the average for a non-Hardwar-Kumbh-Fair year.

North-West Frontier Province.—*Forecast*—cholera low for three years, some increase likely.

Result—prevalence again low except in August.

Sind.—*Forecast*—1931 rains failed so 'in 1932 increased prevalence is likely; this will be liable to reach epidemic proportions if the rains are also short in 1932'.

Result—fortunately the rains were in great excess in July 1932 and there was very little cholera in Sind. This was also largely due to the disease being nearly completely absent from the neighbouring areas of Multan in the south-east Punjab and from Gujerat to the south of Sind from which Sind could be infected. The failure of deficient rains to be followed by a cholera epidemic in the Bombay Presidency in years of very low cholera in India as a whole, such as in 1932, was pointed out in section IV of my memoir of 1928, 1904-1905 having been a typical example. Gujerat also escaped very lightly for the same reason.

Bombay Deccan.—*Forecast*—average to low cholera incidence in 1932.

Result—very little cholera.

Madras Deccan.—*Forecast*—1931 rains rather short, some increase likely over 1931 figures, but not epidemic.

Result—good 1932 monsoon rains and very little cholera, largely due to the disease having been nearly absent from the neighbouring divisions of Madras and the southern Bombay Deccan.

South-East Madras.—*Forecast*—about average incidence.

Result—incidence about the average.

North-East Madras.—*Forecast*—some increase on 1931, low incidence likely in 1932.

Result—low incidence in this division and in the Madras districts south of it.

Central Provinces.—*Forecast*—average to low incidence in 1932.

Result—low incidence.

The above data suffice to show that my forecast was very generally accurate in spite of the year having been a difficult one for that purpose.

Results of smallpox forecast for 1932

General Forecast.—The good 1931 monsoon and normal or high absolute humidities during the monsoon months, and especially in October, throughout north and central India, to which the forecast relates, indicate low smallpox generally in those areas during the smallpox season from October 1931 to September 1932.

* Received by air mail, 1st December, 1932.

Result—low smallpox generally in northern and central India.

United Provinces.—*Forecast*—low smallpox incidence in 1932.

Result—smallpox incidence very low in 1932.

Punjab.—*Forecast*—smallpox in 1932 below the average.

Result—below the average of recent years.

North-West Frontier Province.—*Forecast*—low smallpox incidence in 1932.

Result—about the average of recent years with the highest rates in June and July 1932 with favouring low absolute humidity in April to June 1932.

Central Provinces.—*Forecast*—low incidence in 1932 following very high absolute humidity in 1931 from July to October.

Result—very low smallpox in 1932 with a lower rate, as far as can be judged from the weekly figures alone available, than during the last nine years.

Bombay and Madras Deccan.—*Forecast*—average to low.

Result—low incidence.

Results of plague forecasts for 1932

Bihar and Orissa.—*Forecast*—hot season 1931 temperatures very high and saturation deficiencies high in Bihar, which alone suffers appreciably from plague, so 1932 plague incidence low.

Result—incidence very low, with an unprecedentedly rapid fall in April and May 1932 in relation to exceptional high mean temperatures and saturation deficiencies in March to May.

United Provinces.—*Forecast*—hot weather temperatures and saturation deficiencies very high, incidence likely to be below the average.

Result—incidence low.

Punjab.—*Forecast*—hot season temperature high and unfavourable to plague but saturation deficiencies low and favourable; incidence about average.

Result—incidence about the average of the last few years.

Central Provinces.—*Forecast*—saturation deficiencies and hot season temperature high and unfavourable to plague; 1931-1932 incidence below the average.

Result—about the average of the last few years and higher than in 1930-1931 favoured by very low absolute humidity in October 1931 and rather low mean temperatures in February and March 1932.

Bombay Deccan.—*Forecast*—average to somewhat low incidence.

Result—incidence below average of recent years, but above that of 1930-1932 season with exceptionally low mean temperatures and saturation deficiencies from September 1931 to April 1932.

The plague forecast as a whole therefore has proved unusually accurate, especially when the climatic data subsequent to its issue are taken into account.

Forecast for 1933

(Worked out in London on 18th November, 1932, on climatic data to October received from India.)

General climatic conditions in 1932 to October.—India has once more been favoured with well-distributed monsoon rains in 1932, with moderate defect of 34 per cent. in Bihar, 32 per cent. in the Madras north coast area and the minor defect of 22 per cent. in the east United Provinces. The rainfall was in excess in the North-West Frontier Province and Sind. These conditions are unfavourable to widespread epidemics of cholera or smallpox in India as a whole, but the comparatively low hot-season temperatures and saturation deficiencies in the Deccan and eastern Central Provinces favour increased plague there. In view of the approximately normal climatic data for 1932 in most parts of India, the probable variations from the average of the three epidemic diseases dealt with may be stated briefly as follows.

Probable incidence of cholera in India during 1933

Assam.—1932 rains normal; recent incidence low. *Forecast*—about average incidence in 1933.

Bengal.—Monsoon slight defect of 12 per cent.; low recent incidence. *Forecast*—some increase in 1933 on the incidence of recent years.

Orissa.—June to September rains normal, but October rain low with deficiency in the north Madras districts to the south of Orissa. *Forecast*—increased incidence in 1933.

Bihar.—Monsoon rains to September 34 per cent. deficient, and also low in October; low cholera incidence in last two years. *Forecast*—increased incidence in 1933; this may be considerable if the winter rains are also short. Chota Nagpur will be liable to cholera infection from Bihar and Orissa.

United Provinces.—1932 rains 22 per cent. in defect in the east, but normal in the west; cholera incidence very low in 1932. *Forecast*—increased incidence in 1933, especially in the eastern districts.

Punjab.—1932 rains normal; recent cholera incidence low. *Forecast*—not likely to be epidemic, but some spread from the United Provinces probable.

North-West Frontier Province.—Monsoon in 1932 in excess; low recent prevalence. *Forecast*—not epidemic but may be some spread from the Punjab.

Sind.—1932 rains in considerable excess. *Forecast*—cholera incidence likely to be low.

Guzerat.—Normal rains. *Forecast*—no excess of cholera likely.

Bombay Deccan.—Good rains. *Forecast*—cholera prevalence likely to be average to low.

Central Provinces.—1932 monsoon in moderate excess; very low cholera in 1932. *Forecast*—

average to low prevalence, but probably above that of 1932.

South-East Madras.—Good October rains 1932; incidence low in 1932. *Forecast*—about the average unless the November to January rains are in defect.

North Madras Coast.—Low 1932 monsoon rains; low cholera in 1932. *Forecast*—increased prevalence in 1933, with incidence above the average.

Probable incidence of smallpox in India during 1933

The climatic data available to October 1932 only allow of forecasts of smallpox for north-west and central India for reasons explained in my memoir on the subject. *General.*—The favourable 1932 monsoon, with accompanying average monsoon absolute humidities in most of the areas dealt with, are unfavourable to any greatly increased prevalence of smallpox over the average in north-west and central India as a whole.

Punjab and North-West Frontier Province.—Monsoon absolute humidities from July to September about average, but October readings low. *Forecast*—about average prevalence, but probably some increase on the low 1932 incidence.

Central Provinces.—Monsoon and October absolute humidities normal; very low incidence in 1932. *Forecast*—average to low incidence in 1933.

Bombay and Madras Deccan.—1932 monsoon absolute humidities average in the north Deccan, but high in south Bombay and Madras Deccan. *Forecast*—low smallpox incidence in 1933, especially in the southern Deccan.

Probable incidence of plague in India during 1933

In general low rainfall with high temperatures and saturation deficiencies favour subsequent increased plague, and *vice versa*. The main variations from the normal of these factors and their bearing in plague incidence in the 1932-1933 plague season are as follows.

Bihar.—The hot weather and monsoon temperatures were in considerable excess, as were the saturation deficiencies from January to September 1932. *Forecast*—low plague incidence in the November 1932 to June 1933 plague season.

United Provinces.—Similar climatic conditions prevailed in 1932 in this province to those in Bihar, although to a slightly less degree. *Forecast*—low plague prevalence from November 1932 to June 1933.

Punjab.—Apart from increased saturation deficiency in the hot season the climatic conditions were normal in the Punjab in 1932. *Forecast*—average to low plague incidence in 1933.

(Continued at foot of next column)

THE DURATION OF THE LIFE OF THE EMBRYOS OF *WUCHERERIA BANCROFTI* IN THE HUMAN SYSTEM

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THE nocturnal periodicity of microfilaria in the peripheral blood, and the periodic manifestation of lymphangitis in persons infected with *Wuchereria bancrofti* are occurrences that have long been recognised, though of their cause little is known. That they must be intimately connected with the life-history of the parasite is obvious.

Several explanations have been offered for the nocturnal periodicity of the embryo. Fulleborn (1912) demonstrated that there was a positive attraction, chemical or otherwise, exerted by the Malpighian tubes of the mosquito upon the microfilariae of dogs. Yamada and Yamamoto (1916) considered that the condition could be ascribed to oxygen chemotaxis, and Suganuma (1921) that the most important cause of periodicity was the strong negative heliotropism of the embryo. The last author showed that microfilariae were positively chemotropic to carbon-dioxide, urea, uric acid and grape-sugar, negatively to ammonia and light. Lynch (1919) favoured a mechanical explanation because he noticed that in the collapsed lung of a dog infected with *Dirofilaria immitis* the embryos accumulated in enormous numbers. Yorke and Blacklock (1917) thought it depended primarily upon periodic variations in the arterial supply of larvae to the cutaneous vessels. Recently, Clayton Lane (1929) has contributed his views on the subject and has explained the periodicity by simultaneous cyclical parturition of the female worms and the daily death of the embryos.

A periodicity of recurrence of filarial lymphangitis in filarial subjects is also well

(Continued from previous column)

Central Provinces.—The climatic factors were mostly normal with deficient saturation deficiency favouring increased plague in one quarter. *Forecast*—average to high plague in the August 1931 to May 1933 season, most in the eastern districts bordering on the north Deccan.

Bombay Deccan.—The 1932 hot weather temperatures and saturation deficiencies were low and favourable to subsequent high plague incidence. *Forecast*—increased plague, especially in the north Deccan in the August 1932 to May 1933 season. (The last weekly returns show increased plague here.)

REFERENCE

Rogers, L. (1928). The Incidence and Spread of Cholera in India; Forecasting and Control of Epidemics. *Indian Med. Res. Memoirs*, No. 9.

known. Martinez Alvares (1920) reported a monthly periodicity observed in men and women alike, occurring during the dark phases of the moon, but never at the time of the full moon. A somewhat similar manifestation was observed by Acton and Rao (1930) on some cases of urticaria where the eruption appears periodically. They have suggested in this communication that the periodicity may have something to do with the habits and life-history of the parasite and that further studies may throw some valuable light on this problem.

As yet we know very little about the duration of life of the adult parasite or of its embryos in the human host. The duration of life of the embryos was thought to be a few hours by Myers (1881). Sonsino (1896) determined it as extending over a few days, and Bancroft (1901) as several months. The later work of Fulleborn (1912) on the filariæ of dogs and the transfusion of the blood with microfilariæ of *Dirofilaria repens* into healthy dogs showed that these embryos continue to be present in the system for a period of about three years.

Experiments for observing the duration of life of embryos of *Wuchereria bancrofti* have shown that under aseptic and cool conditions, i.e., in the neighbourhood of 4°C., they can be kept alive for about 4 to 6 weeks outside the body of the host. Our repeated observations made during the last few years have shown that the embryos can be kept alive for varying periods of time after being taken out of the host and that the adults manage to live only for a few hours under the same conditions. This will form the subject of a separate communication. Recently observations have been made which throw light on the probable duration of microfilariæ in the human system; these form the subject of this paper.

The following are the brief notes of the patients who were under observation.

Case I.—N. D., aged 48, Hindu male, a resident of Calcutta, admitted into the Carmichael Hospital for Tropical Diseases in March 1930 for a cyst on the left elbow, about an inch in diameter (figs. 1 and 2). The cyst was quite painless and had developed very slowly; it reached this size in a year's time. The cyst was tapped and 5 c.cm. of clear serous fluid was obtained from it. This fluid on microscopical examination showed innumerable live and active microfilariæ. The peripheral blood taken at midnight showed numerous microfilariæ. After the tapping, the cyst wall collapsed but the cyst had filled again within a few days. The cyst was excised under local anaesthesia. Five entire adult worms were found in the cyst. These findings have been recorded elsewhere (S. Rao, 1930). The peripheral blood was positive for microfilariæ till the time he left the hospital, an interval of five days. Blood examination for microfilariæ was carried out at intervals; it was found that the embryos disappeared completely between the second and the third month after the cyst was excised, and the patient has remained free from embryos since—the last examination of the blood for microfilariæ, made on 2nd September, 1932, showed no embryos.

Case II.—P. A., aged 27, Hindu male, a resident of Pabna (Bengal), admitted into the Carmichael Hospital

for Tropical Diseases on 4th July, 1932, for lymphangitis of the scrotum which ended in the formation of an abscess. Repeated examination of the blood showed no microfilariæ. Small cysts were detected, one on each arm, and on puncture with a hypodermic syringe 0.2



Fig. 1.—Photograph of case 1, showing the location of cyst on the left forearm.

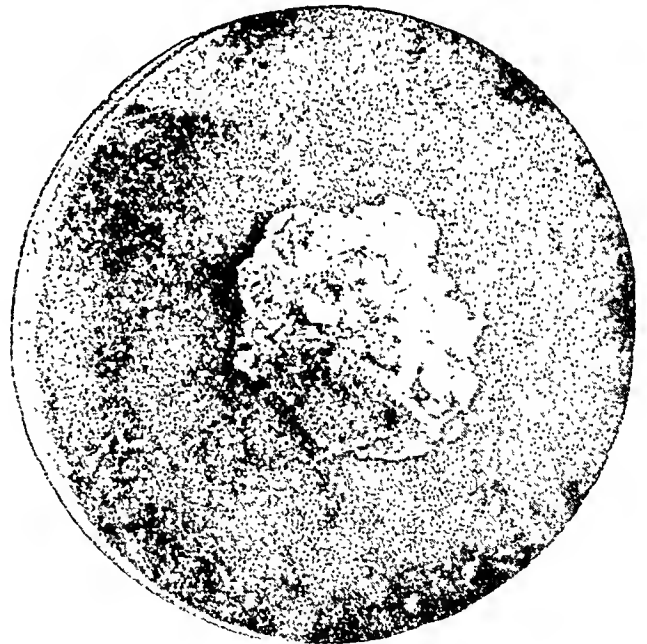


Fig. 2.—Photograph of the cyst from case 1.

and 0.3 c.cm. of clear whitish fluid was drawn from each of them. The fluids from the cysts on microscopic examination showed a few microfilariæ in each. The cyst in the right axilla (fig. 3) was excised under local anaesthesia on 22nd July and several mature and immature worms, similarly actively moving inside the cyst, were collected. The second cyst on the left arm (fig. 3) was excised on 4th August and from this again

six adult worms were recovered. The peripheral blood, which was 'negative' till 4th August, showed microfilariae and table I shows the microfilariae count per 100 c.mm. of blood taken from the finger every 24 hours



Fig. 3.—Photograph of case 2, showing the location of the cysts on both the arms.

at midnight. From October 13th onwards the blood has remained entirely free from microfilariae, though examinations were continued for 37 days.

the blood is negative. So that, in both the cases, there is definite evidence of the cyst being the location of the adult worms and the sole source of embryos in the blood. As soon as the main colony of the adults and embryos was taken out by surgical operation, the few embryos which were able to get into the blood stream appear to have survived for about 70 days. At the end of this period they seem to have died out and disappeared completely. It seems therefore reasonable to draw the inference that the duration of life of the embryo coincides with the above period. It is evident that some of the embryos circulating in the peripheral blood at the time when the cysts were removed would be older than others, but the fact that at the end of about 70 days all have disappeared shows that the youngest of these have survived this period before finally dying out. The second case is still under observation so that it should be possible in the near future to confirm or refute the view about periodicity expressed above.

In this connection it may be pointed out that there is a certain element of uncertainty in relying on blood examination alone, because on certain occasions cases known to have large

TABLE I

Date	Microfilariae per 100 c.mm.	Date	Microfilariae per 100 c.mm.	Date	Microfilariae per 100 c.mm.	Date	Microfilariae per 100 c.mm.	Date	Microfilariae per 100 c.mm.
6-8-32	4	20-8-32	1	3-9-32	1	17-9-32	0	1-10-32	0
7-8-32	3	21-8-32	3	4-9-32	0	18-9-32	1	2-10-32	2
8-8-32	4	22-8-32	0	5-9-32	0	19-9-32	0	3-10-32	0
9-8-32	2	23-8-32	1	6-9-32	1	20-9-32	0	4-10-32	0
10-8-32	2	24-8-32	0	7-9-32	0	21-9-32	1	5-10-32	0
11-8-32	3	25-8-32	0	8-9-32	1	22-9-32	0	6-10-32	1
12-8-32	2	26-8-32	3	9-9-32	2	23-9-32	0	7-10-32	1
13-8-32	1	27-8-32	1	10-9-32	0	24-9-32	1	8-10-32	0
14-8-32	2	28-8-32	1	11-9-32	0	25-9-32	0	9-10-32	0
15-8-32	3	29-8-32	0	12-9-32	0	26-9-32	0	10-10-32	0
16-8-32	0	30-8-32	0	13-9-32	0	27-9-32	0	11-10-32	0
17-8-32	1	31-8-32	0	14-9-32	0	28-9-32	0	12-10-32	2
18-8-32	1	1-9-32	0	15-9-32	0	29-9-32	1	13-10-32	0
19-8-32	2	2-9-32	2	16-9-32	0	30-9-32	2	14-10-32	0

There are also on our records several other cases where the appearance and disappearance of microfilariae in the blood show a regular periodicity. Since regular observations have not been made on these cases, they are not described here.

Discussion of observations

In the cases described above, the blood examination gave positive results for a certain period and then became negative. In the second case observations were carried out systematically, the embryos being present in the peripheral blood for a period of 70 days and then disappearing. The microfilariae appeared in the blood stream soon after the second cyst was cut out and then disappeared; up to the time of writing this communication

numbers of microfilariae in their blood may be completely negative. It is of course well known that the blood in cases of *Wuchereria bancrofti* infection has to be taken for examination at midnight to ensure getting definite proof of the infection. The cases cited above and numerous others in our records show that there may be great variations in the number of embryos found in the peripheral blood in different individuals at different times, though they may all be equally infected. Till the life-history of the parasite is thoroughly worked out it will not be possible to be positive about the duration of life of the embryos, for, even when experimenting with volunteers, it will be necessary first of all to know the age of the embryo before we can draw reliable conclusions.

(Continued at foot of next page)

THE TREATMENT OF CHRONIC INTES- TINAL AMOEBIASIS WITH THE ALKA- LOIDS OF *HOLARRHENA ANTIDYSEN- TERICA* (KURCHI)

By HUGH W. ACTON, C.I.E.

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CHOPRA and others (1927) have shown that the alkaloids of *Holarrhena antidysenterica* possess marked amœbicidal properties, and Ghosh and Ghosh (1928) have shown that the Indian species of *H. antidysenterica* contain, besides *conessine*, two other alkaloids which they named *kurchicine* and *kurchine*, respectively. Ghosh and Bose (1932) isolated these alkaloids in pure form and showed that the alkaloid, *kurchine*, is characterised by having a low melting point at 75°C., and that it is the most abundant alkaloid in the bark. Acton and Chopra (1929) pointed out that these alkaloids can be used in the treatment of amœbic dysentery in man. In contradistinction to emetine, they have no depressant, emetic or toxic properties, and their preparations can be

given by the mouth in fairly large doses without producing untoward effects. In acute amœbic dysentery intramuscular injections of two grains of the total alkaloids produced disappearance of *E. histolytica* from the stools as quickly as did emetine; they, however, produced severe irritation and pain at the site of injection, and all our efforts to produce compounds which would be less irritant were unsuccessful. These alkaloids, however, do not produce the other toxic effects of emetine, and, as soon as a non-irritant salt is prepared, their use in the treatment of acute intestinal amœbiasis will undoubtedly be extended.

For chronic intestinal amœbiasis, for reasons we have already discussed, it is preferable to give the alkaloids by the mouth, and we prepared and used a bismuthous iodide compound of the total alkaloids; this we called *kurchi bismuthous iodide*. This compound was originally prepared in 1928 on the same lines as emetine bismuth iodide. Its approximate composition is as follows:—total alkaloids, 27 per cent., bismuth, 22.85 per cent., and iodine, 50.15 per cent. Soon after these facts were published a number of firms started manufacturing the compound and put it on the market under various trade names. The latter fact is to be greatly regretted as the name *kurchi bismuthous iodide* is much more expressive and gives the practitioner a better idea as to what he is using than do the fancy names, which convey nothing and only create confusion. This compound can be administered in doses of 10 grains twice daily for ten to twenty days without any deleterious effects. Such doses cured a large number of chronic cases of intestinal amœbiasis which had proved resistant to treatment with emetine and other drugs. In a case of commencing liver abscess, however, Chopra and De (1930) found that injections of the alkaloids were ineffective.

For the last three years the authors have tried *kurchi bismuthous iodide* in a large number of cases, both inside and outside the hospital, with very satisfactory results. Complete records are available of a series of 77 cases treated in the Carmichael Hospital for Tropical Diseases and a summary of these is given in the appendix.

Before going into the details of these cases it is necessary to explain the somewhat discordant results obtained by different clinicians in the treatment of chronic intestinal amœbiasis with *kurchi bismuthous iodide*. We were ourselves considerably puzzled by contradictory findings for a long time. It must be stated here that, in the early trials with this compound, the isolation of the alkaloids and the preparation of the bismuthous iodide compound was carried out entirely in the Department of Chemistry of the School under the direct supervision of Dr. S. Ghosh, the Professor of Chemistry. With this preparation our results were uniformly good. The process of preparation was then given over to some of the local

(Continued from previous page)

In conclusion, the writer wishes to express his thanks to Lieut.-Colonel H. W. Acton, C.I.E., I.M.S., Director, Calcutta School of Tropical Medicine, for his active interest in the work and constant encouragement.

REFERENCES

- Acton, H. W., and Rao, S. S. (1930). Urticaria due to Filarial toxin. *Indian Med. Gaz.*, Vol. LXV, p. 130.
- Alvarez, A. M. (1920). Observations on Filariasis. *New Orleans Med. and Surg. Journ.*, Vol. LXXII, p. 701.
- Bancroft, T. L. (1901). Quoted from *Handbuch der Tropenkrankheiten*, by C. Mense, Band V, Part I, 3rd Edn., p. 267, Leipzig; Johann Ambrosius Barth, 1929.
- Fulleborn, F. (1912). Beiträge zur Biologie der Filarien. *Centralbl. Bakt.*, Band LXVI, p. 255.
- Fulleborn, F. (1912). Untersuchungen über die Chemotaktische Wirkung der Malpighischen Gefäße von Stechmücken auf Hundemikrofilarien. *Centralbl. Bakt.*, Band LXV, p. 349.
- Lane, C. (1929). The Mechanism of Filarial Periodicity. *Lancet*, Vol. I, p. 1291.
- Lynch, K. M. (1919). Filarial Periodicity. *Journ. Amer. Med. Assoc.*, Vol. LXXIII, p. 760.
- Myers (1881). Quoted from *Handbuch der Tropenkrankheiten*, by C. Mense, *vide supra*.
- Suganuma, S. (1921). Contributions to the knowledge on the Periodicity of the *Filaria bancrofti*. *Japan Med. World*, Vol. I, p. 1.
- Sonsino (1896). *Handbuch der Tropenkrankheiten*, by C. Mense, *vide supra*.
- Rao, S. S. (1930). Records of Findings of Adult *Wuchereria (Filaria) bancrofti* in India. *Indian Med. Gaz.*, Vol. LXV, p. 481.
- Yamada, M., and Yamamoto, T. (1916). Quoted from *Trop. Dis. Bull.*, 1917, Vol. X, p. 275.
- Yorke, W., and Blacklock, B. (1917). Observations on the Periodicity of *Microfilaria nocturna*. *Ann. Trop. Med. and Parasit.*, Vol. XI, p. 127.

manufacturers and we started using their product in the treatment of our patients in the hospital. For a time all went well, but, after a particular preparation was started, practically all the patients under this treatment remained uncured. On investigation it was discovered that the process of manufacture described by us had been modified, and in order to facilitate the extraction of the alkaloids, hot alcohol had been used instead of the cold as originally recommended. This had the effect of changing the alkaloids, and possibly radical changes were produced in the one with a low melting point which forms the chief constituent. This was rectified and our results considerably improved for a time. In the meantime the demand for kurchi bismuthous iodide increased enormously, and after a while we again started getting failures in almost all our patients treated with this compound. On further investigation and careful survey of all the facts we came to the conclusion that this time the failures were to be attributed to the fact that the supply of good fully-matured bark could not keep pace with the large demand and that consequently large quantities of immature, improperly-collected and imperfectly-dried bark were coming into the market. Such bark was being employed for the extraction of the alkaloids used in the preparation of kurchi bismuthous iodide. To confirm this view we obtained matured and properly-collected bark from Assam, and prepared the bismuthous iodide compound from this material in our laboratory. Of a series of 13 cases treated with this preparation 10 (76.92 per cent.) were cured and 3 (23.08 per cent.) failed. The discordant results, in our opinion so far as kurchi bismuthous iodide is concerned, are due to :—

1. Some fault in the procedure of extraction of the alkaloids from the bark or preparation of the compound, e.g., use of hot alcohol instead of cold.

2. The bark from which the alkaloids are extracted not being mature, being improperly collected, or being imperfectly dried.

Besides these, there are two other factors which have an important bearing on the curative effects produced by this compound. Firstly, it is well known that in some of the chronic cases of amoebiasis there is mixed infection with bacillary dysentery also. The bacterial cultures from the stools of such patients show various non-lactose-fermenting organisms which complicate matters and delay cure. The isolation of these organisms is often a difficult matter and they are missed unless repeated examinations of stools are made by an expert bacteriologist. In such cases, unless a course of vaccines is given as a preliminary to treatment with the bismuthous iodide compound, the chances of cure are not so favourable. In some of our cases where such a state of affairs existed, a course of autogenous vaccines, preceding the treatment with kurchi bismuthous

iodide, often produced cures where the drug alone failed. The patients with mixed infections are much more resistant to treatment than simple cases.

Secondly, the reaction of the gut contents is often strongly acid in chronic intestinal amoebiasis and the action of these alkaloids is considerably weakened on this account. By administering kurchi bismuthous iodide with large doses of alkalies the chances of cure are greatly enhanced. The routine treatment followed in most of our patients was to give a mixture consisting of one drachm of sodium bicarbonate and 40 grains of sodium citrate half an hour before each dose of the bismuthous iodide.

The compound itself was given in doses of 10 grains administered twice daily for ten consecutive days. One such course sufficed to produce a cure in the majority of cases of chronic intestinal amoebiasis and *E. histolytica*, both vegetative and cystic forms, disappeared from the stools. The patient is kept on ordinary diet, no strict dieting being necessary except when the relapse is very acute. Sometimes, a second course is necessary. As these alkaloids are rapidly excreted from the body, and, unlike emetine, do not produce any cumulative toxic effects, the second course can be given immediately following the first course. Often it is not necessary to give a complete second course of ten days, only half a course, i.e., administration of the drug for fifteen days altogether, sufficing. Our experience is that in simple cases where there is no infection with bacillary dysentery, a ten-days' course cures a large number of cases, but when a mixed infection is present a course of 15 to 20 days is necessary. Even after a course of 20 days a number of cases prove resistant to treatment. Some of these yield to treatment with emetine bismuthous iodide, others do not. For this latter group we do not recommend another course of kurchi bismuthous iodide, but prolonged treatment with standardised extract of kurchi (containing half a grain of the total alkaloids in one drachm) often produces satisfactory results. One to two drachms of the extract are given twice daily for three months or even longer if necessary. Such doses do not produce any toxic effects and cure about 50 per cent. of the obstinate and persistent cases.

The extract may be given by itself or may be combined with *Plantago ovata* (Isabgul). The two drugs can be given concurrently, or alternately for ten days at a time, *Plantago ovata* being given in doses of 1 to 2 heaped tablespoonfuls, once or twice daily. Chopra (1930) showed that the action of the seeds is mechanical, and due to the large quantities of the mucilage which is contained in the superficial layers of the seeds. This covers the ulcers and protects them from the irritating contents of the intestines, solids, fluids and gases, in this way enabling the lesions to heal

quickly. Further, the gel formed from the seeds inhibits the growth of intestinal bacteria and adsorbs the toxins formed by them, thus preventing them from being absorbed into the system.

We have not met with any serious toxic or cumulative effects from the use of either the extract, the alkaloids, or kurchi bismuthous iodide, in the doses stated above. As much as six grains of the alkaloids were given by the mouth for 10 to 20 consecutive days without producing untoward effects. Rarely, flushing of the face and extremities, buzzing in the head and giddiness were produced, especially in the European patients, but these passed off when the dose was reduced. The taste of the alkaloids is very bitter and some patients object to it. This can be avoided by giving the compound in capsules or in tablet form.

The criterion of cure applied by us in this series was five or more negative examinations of the stools on different days after the cessation of all treatment. It is fully realised that it cannot be claimed from this that all such cases were really cured, but it is the best criterion that can be employed and from experience we know that 5 negative examinations indicate a favourable prognosis. The difficulty of keeping the patient in the hospital, when once the acute symptoms are relieved, is very great, so for practical purposes we had to accept this criterion. Whenever possible more examinations were made and in some as many as 10 or 12 stools were examined. If either vegetative or the encysted forms of *E. histolytica* were found in the stools after the cessation of treatment it is clear that the infection was not eradicated. Such cases mean entire failure of treatment. The 'indeterminate' cases were those in which less than five stools could be examined after cessation of all the treatment owing to the patient leaving the hospital earlier. It is impossible to say whether such cases will or will not relapse.

The appendix is self explanatory. A perusal of it will show that in all 78 cases of intestinal amœbiasis were treated with kurchi bismuthous iodide, in the Carmichael Hospital for Tropical Diseases during the last three years. Many of these patients gave a history of dysentery lasting for many years, and had cystic forms of *E. histolytica* and Charcot-Leyden crystals in their stools. In this series it will be observed that with the criterion of cure laid down above, 57 patients or 73 per cent. were cured, 3 or 3.84 per cent. were indeterminate, and 18 or 23.1 per cent. failed to be cured. The proportion of probable cures to failures in this series is 3.16:1, as compared with 1:3.5 obtained by Knowles (1928) with emetine bismuthous iodide in similar chronic cases. A further study of the appendix will show that out of 42 patients who had cystic forms of *E. histolytica* in the stools, 31 were cured and 11 failed, the ratio of probable cures to failures here being 2.8:1.

Among the failures, it is interesting to note that 11 had only cystic forms and seven vegetative forms of *E. histolytica* before treatment; some of the former (nos. 42, 48, 64, and 78) subsequently received emetine treatment and still remained uncured. It was further observed that, in the patients with vegetative forms of *E. histolytica*, the vegetative form was often converted into the cystic form after unsuccessful treatment with the bismuthous iodide compound. The probable explanation is that these alkaloids make the gut wall an unfavourable abode for these protozoa which then develop into the cystic stage. This fact lends an indirect support to the view that the alkaloids of *H. antidyenterica* are toxic to *E. histolytica*.

The last five cases in the series were very resistant cases of mixed infection and were treated both with vaccines and kurchi bismuthous iodide. Three out of five cases were cured and two failed.

Summary and conclusions

1. The alkaloids of *H. antidyenterica* are powerful curative agents in intestinal amœbiasis. In acute amœbic dysentery intramuscular injections of 2 grains daily of the hydrochloride produce a cure as rapidly as emetine, but they are very painful.

2. The bismuthous iodide compound of the total alkaloids is an effective remedy against chronic intestinal amœbiasis. The proportion of probable cures to failures in a series of 78 cases was 3.16:1, which compares favourably with Knowles series with emetine bismuth iodide, in which this ratio was 1:3.5.

3. The bismuthous iodide should be administered in doses of 10 grains twice daily preceded half an hour by a mixture containing one drachm of sodium bicarbonate and 40 grains of sodium citrate. No strict dietary measures are necessary unless the relapse is of a very acute nature.

4. In simple cases, where there is no mixed infection with bacillary dysentery, a course of ten days' duration cures a large number of patients. When a mixed infection exists a course of 15 to 20 days may be necessary. A second course is not desirable.

5. In obstinate and persistent cases resisting treatment, a prolonged course (3 months or more) of standardised extract of kurchi 1 to 2 drachms twice daily, with or without *Plantago ovata* (Isabgul) is often effective.

6. When mixed infections exist a course of autogenous vaccines should precede the treatment with the kurchi bismuthous iodide compound.

We are very grateful to Dr. B. Sen, B.Sc., M.B., for his help in collecting and analysing the case notes.

REFERENCES

Acton, H. W., and Chopra, R. N. (1929). Kurchi bismuth iodide, its value in the treatment of chronic amoebic infections of the bowel. *Indian Med. Gaz.*, Vol. LXIV, p. 481.

Chopra, R. N. (1930). *Plantago ovata*—Ispaghul—in chronic diarrhoeas and dysenteries. *Indian Med. Gaz.*, Vol. LXV, p. 428.

Chopra, R. N., Gupta, J. C., David, J. C., and Ghosh, S. (1927). Observations on the pharmacological action of conessine, the alkaloid of *Holarrhena antidysenterica*. *Indian Med. Gaz.*, Vol. LXII, p. 132.

Chopra, R. N., and De, N. (1930). The failure of the alkaloids of *Holarrhena antidysenterica* (kurchi) in the treatment of amoebic hepatitis. *Indian Med. Gaz.*, Vol. LXV, p. 391.

Ghosh, S., and Bose, I. (1932). Die Alkaloide der Rinde von *Holarrhena antidysenterica* (kurchi bark). Zweiter Teil. *Arch. Pharm.*, Vol. CCLXX, p. 100.

Ghosh, S., and Ghosh, N. N. (1928). The alkaloids of kurchi bark (*Holarrhena antidysenterica*). Part I. *Journ. Indian Chem. Soc.*, Vol. V, p. 477.

Knowles, R., Das Gupta, B. M., Dutta Gupta, A. K., and Gupta, U. (1928). The treatment of intestinal amoebiasis (an analysis of results and a review of the literature). *Indian Med. Gaz.*, Vol. LXIII, p. 455.

APPENDIX

(Cases treated with Alkali and Kurchi Bismuthous Iodide)

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
1	K. M. H.	M., M., 24	10 months, 2 emetine.	<i>E. h.</i> veg. and cyst.*	B. K. I. gr. x, b.d., 10 days.	<i>E. h.</i> veg. and cyst.	Failed.
2	Mastakin	M., M., 18	2 weeks	<i>E. h.</i> veg., H. W. ova.	Do.	Negative 6 exams.	Cured.
3	De Munter	E., M., 29	2 months	<i>E. h.</i> cyst	Do.	<i>E. h.</i> veg.	Failed.
4	Mawson	E., F., 29	3 weeks	<i>E. h.</i> veg.	Do.	<i>E. h.</i> cyst.	"
5	F. M.	M., M., 25	5 months	Do.	B. K. I. grs. x, b.d., 10 days. T.A.K. gr.i.	Scanty <i>E. h.</i> cyst.	"
6	Harris	A. I., M., 27	4 years. Emetine outside.	<i>E. h.</i> veg. and cyst. C. L. crystals. <i>E. nana</i> cysts. Blastocystis.	Do.	Negative 6 exams.	Cured.
7	Asrumoy	H., M., 6	3 years	<i>E. nana</i> cysts, Blastocystis.	B. K. I. grs. iii, b.d., 10 days.	Negative 7 exams.	"
8	Mcgregor	E., M., 24	1 month	<i>E. h.</i> cysts, C. L. crystals.	B. K. I. grs. x, b.d., 10 days.	Negative 6 exams.	"
9	Sumaria	H., F., 30	2 months	Scanty <i>E. h.</i> veg.	B. K. I. grs. vii, b.d., 10 days.	Do.	"
10	R. B.	H., M., 60	2 weeks; in-patient 3 months ago for amoebiasis and was cured.	<i>E. h.</i> veg. Trichomonas.	B. K. I. grs. x, b.d., 10 days.	Do.	"
11	D.	H., F., 30	Chronic dysentery	<i>E. h.</i> veg. and cyst	Do.	<i>E. h.</i> cyst	Failed.
12	C. S.	A. I., M., 5	A case of K. A. with <i>E. h.</i>	Scanty <i>E. h.</i> cyst	B. K. I. grs. iii, 3 days, grs. ii, 7 days.	Negative 4 exams.	Cured.
13	P. K. B.	H., M., 27	Dysentery since childhood.	<i>E. h.</i> veg. and cyst	B. K. I. grs. x, b.d., 10 days.	Negative 10 exams.	"
14	N. D.	H., M., 40	2 years. 6 emetine outside.	<i>E. h.</i> veg.	Do.	Negative 6 exams.	"
15	Marchant	A. I., F., 32	1 year	<i>E. h.</i> veg. scanty	Do.	Do.	"
16	Ram	H., M., 45	10 days	<i>E. h.</i> veg. H. W. ova. Trichomonas.	Do.	Negative 2 exams.	Indeterminate.
17	N. N.	H., M., 34	5 years off and on. Present attack 10 days.	Scanty <i>E. h.</i> veg. C. L. crystals.	B. K. I. grs. x, b.d., 15 days.	Negative 9 exams., from the 6th day of B. K. I.	Cured.
18	M. H.	M., M., 24	1 year	<i>E. h.</i> cyst, <i>E. nana</i> cyst and Blastocystis.	Do.	Negative 10 exams., from the 5th day of B. K. I.	"
19	De Munter	E., M., 29	Chronic dysentery	Scanty <i>E. h.</i> cyst. Scanty <i>E. nana</i> cyst.	B. K. I. grs. x, b.d., 20 days, injection T.A.K. gr.i, 5 days.	Negative 7 exams.	"

* See list of abbreviations at end of appendix.

APPENDIX—contd

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
20	S. K. C. ..	H., M., 19	Chronic dysentery	Scanty <i>E. h.</i> cyst	B. K. I. grs. x, b.d., 10 days.	Negative 11 exams.	Cured.
21	U. S. ..	H., M., 30	2 years, emetine outside.	<i>E. h.</i> veg. <i>B. lactis acrognes.</i>	Do.	Negative 10 exams.	"
22	Jana ..	H., M., 25	4 years	<i>E. h.</i> veg. and cyst	Do.	Negative 12 exams.	"
23	Young ..	E., M., 31	3 years. Much emetine outside.	Scanty <i>E. h.</i> veg.	B. K. I. grs. x, b.d., 20 days. T. A. K. gr. i daily 5 days.	Negative 6 exams.	"
24	Fellwood	E., M., 51	Pityriasis rubra and chronic dysentery.	<i>E. h.</i> cyst	B. K. I. grs. x, b.d., 10 days.	Negative 8 exams.	"
25	Peters ..	A. I., F., 45	1 year	<i>E. h.</i> veg.	Do.	Negative 7 exams.	"
26	Cronkite	E., F., 35	Do.	Do.	Negative 6 exams.	"
27	Adhikari	H., M., 56	Psoriasis and chronic dysentery.	Do.	Do.	Do.	"
28	Saker ..	E., F., 31	Chronic dysentery	Few <i>E. h.</i> cyst	Do.	Do.	"
29	Jones ..	A. I., M., 58	1 year	Scanty <i>E. h.</i> cyst	B. K. I. grs. x, b.d., 15 days.	Negative 11 exams.	"
30	B. A. ..	H., M., 30	8 years	<i>E. h.</i> veg.	B. K. I. grs. x, b.d., 10 days.	Do.	"
31	H. I. A. ..	Jew, F., 37	3 years. Stovarsol 4 months ago.	Record mislaid	Do.	Negative 6 exams., clinical improvement.	"
32	A. K. P. ..	H., M., 62	14 years	<i>E. h.</i> cyst	Do.	Negative 12 exams.	"
33	Nemai ..	H., M., 18	1 year	<i>E. h.</i> veg. and cyst. <i>Giardia.</i>	Do.	Negative 8 exams.	"
34	B. S. ..	H., M., 20	Epidemic dropsy and chronic dysentery.	<i>E. h.</i> and <i>I. butschlii</i> cyst.	Do.	Negative 6 exams.	"
35	D. Winn	A. I., M., 49	7 months. Many emetine.	<i>E. h.</i> cyst	B. K. I. grs. x, b.d., 15 days.	Negative 8 exams.	"
36	K. D. ..	H., M., 50	2 years	<i>E. h.</i> veg.	B. K. I. grs. x, b.d., 10 days.	Negative 5 exams.	"
37	A. S. D. T.	E., M., 30	2 years	Scanty <i>E. h.</i> cyst	Do.	Scanty <i>E. h.</i> veg. and cyst.	Failed.
38	Smith ..	E., F., 40	1 year. Emetine with no effect.	<i>E. h.</i> cyst	Do.	Negative 7 exams.	Cured.
39	D. R. ..	H., M., 28	K. A. and chronic dysentery.	<i>E. h.</i> cyst and <i>Blastocystis.</i>	Do.	Negative 9 exams.	"
40	R. C. J. ..	E., M., 25	<i>E. h.</i> cyst	Do.	Negative 5 exams.	"
41	T. K. ..	H., M., 23	K. A. and chronic dysentery.	Scanty <i>E. h.</i> veg.	B. K. I. grs. x, b.d., 10 days.	Negative 8 exams.	"
42	R. F. A. ..	E., M., 62	6 weeks	No <i>E. h.</i> <i>Trichomonas</i> , few C. L. crystals.	B. K. I. grs. x, b.d., 15 days, afterwards 6 emetine.	<i>E. h.</i> veg. and cyst and <i>Trichomonas</i> present.	Failed.
43	A. C. ..	H., M., 38	Diabetes and chronic dysentery.	Scanty <i>E. h.</i> cyst and <i>E. nana</i> cyst.	B. K. I. grs. x, b.d., 10 days.	Negative 11 exams.	Cured.
44	A. R. ..	H., M., 22	Scanty <i>E. h.</i> veg. and <i>E. nana</i> cyst. <i>Trichomonas</i> and <i>Blastocystis.</i>	B. K. I. grs. x, b.d., 4 days.	Left after 4 days.	Indeterminate.
45	Emmer ..	A. I., F., 19	Pain right iliac region 2½ years.	<i>E. h.</i> veg. and cyst	B. K. I. grs. x, b.d., 10 days.	Negative 3 exams.	"
46	Shakespeare	A. I., F., 26	11 months emetine outside.	<i>E. h.</i> veg. and cyst. <i>Blastocystis.</i>	Do.	<i>E. h.</i> veg. and cyst.	Failed.
47	S. J. ..	M., M., 40	3 years	<i>E. h.</i> veg. C. L. crystals.	B. K. I. grs. x, b.d., 20 days.	Negative 8 exams.	Cured.

APPENDIX—*contd*

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
48	A. V. ..	E., M., 34	5 years	Scanty <i>E. h.</i> cyst, <i>E. nana</i> veg. and cyst, and Blastocystis.	B. K. I. grs. x, b.d., 4 days; then grs. vii for 2 days. E. B. I. grs. ii in Liq. paraffin 10 days.	<i>E. h.</i> veg. and cyst.	Failed.
49	E. Gall ..	E., M., 30	18 months	<i>E. h.</i> veg.	B. K. I. grs. x, b.d., 10 days.	<i>E. h.</i> cyst	"
50	C. W. ..	E., M., 10	K. A. and Chronic dysentery.	<i>E. h.</i> veg. and cyst. Blastocystis.	B. K. I. grs. v, b.d., 10 days.	Negative 6 exams.	Cured.
51	R. A. ..	I. Ch., M., 7	K. A. and dysentery 2 years.	<i>E. h.</i> veg. and cyst	Do.	<i>E. h.</i> veg. and cyst. Giardia cysts.	"
52	S. B. ..	H., M., 12	Chronic dysentery	<i>E. h.</i> veg. and cyst. Blastocystis.	B. K. I. grs. v, b.d., 4 days. B. K. I. grs. vii, b.d., 10 days.	<i>E. h.</i> veg. and cyst. Blastocystis.	Failed.
53	Moris ..	A. I., F., 26	Do.	Scanty <i>E. h.</i> cyst	B. K. I. grs. x, b.d., 10 days.	Negative 7 exams.	Cured.
54	B. B. ..	M., H., 15	K. A. and chronic dysentery.	<i>E. h.</i> veg. and Trichomonas.	Do.	Negative 6 exams.	"
55	Ezekiel ..	Jew, F., 27	5 years	<i>E. h.</i> veg.	B. K. I. grs. x, b.d., 3 days and grs. vii 7 more days.	Do.	"
56	Casey ..	A. I., F., 28	2 years	Scanty <i>E. h.</i> veg. Blastocystis, <i>B. faecalis alk.</i>	B. K. I. grs. x, b.d., 10 days.	Do.	"
57	Good ..	A. I., M., 23	Malaria and chronic dysentery.	Scanty <i>E. h.</i> veg. and cyst. <i>C. L.</i> crystals; <i>B. faecalis alk.</i>	Do.	Negative 6 exams.	"
58	Curry ..	E., F., 38	2 years	<i>E. h.</i> veg. and cyst, Blastocystis, <i>I. butschlii</i> cysts.	Do.	<i>I. butschlii</i> cysts present. Blastocystis. Negative 6 exams.	"
59	Loiscan ..	A. I., F., 5	Attack 2 weeks ago.	<i>E. h.</i> veg.	B. K. I. grs. iii, b.d., 10 days.	Negative 6 exams.	"
60	S. Roy ..	H., F., 40	6 to 18 months; 3 months very bad.	<i>E. h.</i> veg.; H. W. ova.	B. K. I. grs. x, b.d., 10 days.	Negative 7 exams.	"
61	Ferron ..	A. I., F., 43	2 years	Scanty <i>E. h.</i> cyst	Do.	Negative 4 exams.	"
62	C. E. K. ..	A. I., M., 53	Pyodermia Mansonii. Chronic dysentery.	Scanty <i>E. h.</i> veg. and cyst. <i>E. nana</i> .	B. K. I. grs. x, b.d., 18 days.	<i>B. faecalis alk.</i> Scanty <i>E. h.</i> veg. present.	Failed.
63	Ezra ..	Jew, F., 55	2 years. Emetine	<i>E. h.</i> veg.	B. K. I. grs. x, b.d., 10 days.	<i>E. h.</i> veg. and cyst.	"
64	P. Das ..	H., M., 44	6 years; worse 2 months.	<i>E. h.</i> cyst, Chilomastix veg., Blastocystis, H. W. ova.	B. K. I. grs. x, b.d., 15 days.	<i>E. h.</i> veg. and cyst. <i>E. nana</i> cysts. Chilomastix veg. and cyst.	"
65	S. Dasi ...	H., F., 32	1 year	<i>E. h.</i> and <i>E. nana</i> cysts, Blastocystis.	Emetine gr. i, 6 days. E. B. I. grs. ii, daily 10 days with omnopon gr. 1/6.	<i>E. h.</i> veg.	"
66	Bacon ..	E., M., 49	4 years. Suffered since 1907.	<i>E. h.</i> cyst, <i>E. nana</i> and <i>E. coli</i> cyst	B. K. I. grs. x, b.d., 9 days.	Negative 5 exams. Scanty <i>E. h.</i> cyst in sample sent later.	"

APPENDIX—concl'd

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
67	Patra ..	H., M., 18	Malaria and chronic dysentery.	<i>E. h. veg.</i>	B. K. I. grs. iv, b.d., 10 days.	Negative 6 exams.	Cured.
68	Izad Bux ..	M., M., 24	<i>E. h.</i>	B. K. I. grs. x, b.d., T. A. K. gr. i, 10 days.	Negative 5 exams.	"
69	Mekie ..	E., M., 48	Dysentery since 8-1-30.	Scanty <i>E. h. veg.</i>	B. K. I. grs. x, b.d., 28 days. Kurchi extract 1 dr., b.d., 30 days.	Negative 6 exams.	"
70	Langlin ..	E., F., 30	5 years	<i>E. h. cyst</i>	B. K. I. grs. x, b.d., 10 days.	Negative 7 exams.	"
71	M. D. D.	M., M., 25	9 years. Emetine, stovarsol, yatren tried.	Do.	B. K. I. grs. x, b.d., 15 days.	Negative 6 exams.	"
72	S. M. ..	M., M., 56	Pain neck and shoulder and low fever for 15 days.	Scanty <i>E. h. veg.</i> and cyst. H. W. and Trichuris ova.	B. K. I. grs. x, b.d., 10 days, and T. A. K. gr. i, 10 days.	Do.	"
73	Kalipada	H., M., 22	1 year. Emetine. Chronic dysentery.	Scanty <i>E. h. veg.</i> , C. L. crystals, <i>B. lactis aerogenes</i> .	B. K. I. grs. x, b.d., 10 days.	Negative 5 exams.	"
74	M. J. ..	I. Ch., F., 39	Asthma and chronic dysentery.	Scanty <i>E. h. cyst</i>	B. K. I. grs. vii, b.d., 10 days. Autovac. B. K. I. grs. x, b.d., 15 days.	Scanty <i>E. h. veg.</i> Negative 10 exams.	"
75	Smith ..	F., E., 40	1 year. Emetine	<i>E. h. cyst</i> and opaque non-lac. fermenters.	B. K. I. grs. x, b.d., 10 days and 6 injections of auto-vaccine.	Negative 7 exams.	"
76	A. J. ..	A. I., M., 29	Present attack 10 days. Had another attack 2 months ago. Emetine.	<i>E. h. cyst.</i> C. L. crystals, H. W. ova.	B. K. I. grs. x, b.d., 10 days.	Negative 6 exams.	"
77	Fitzpatrick	E., M., 39	13 months	<i>E. h. veg.</i> and <i>B. pseudo-carolinus</i> .	B. K. I. grs. x, b.d., 15 days and 6 auto-vaccine.	<i>E. h. cyst</i> and C. L. crystals.	Failed.
78	Gassin ..	A. I., M., 45	10 years	Scanty <i>E. h. veg.</i> and feeble lactose fermenters.	B. K. I. grs. x, b.d., 17 days. E. B. I. grs. ii, in paraffin 2 days. B. K. I. grs. x, b.d., 15 days, 6 emetine and 3 stock vaccine. Ext. kurchi liq., 2 days.	<i>E. h. veg.</i> and cyst.	"

Abbreviations used:—

A. I. = Anglo-Indian. H. W. = Hookworm.
 E. = European. *E. h.* = *Entamoeba histolytica*. C. L. crystals = Charcot-Leyden crystals.
 H. = Hindu. Veg. = Vegetative. B. K. I. = Kurchi bismuthous iodide.
 M. M. = Mohammedan Male. Cyst. = Cystic. E. B. I. = Emetine bismuthous iodide.
 M. F. = Mohammedan Female. K. A. = Kala-azar. T. A. K. = Total alkaloids of kurchi.
 Emetine and T. A. K. were injected intramuscularly; 6 emetine gr. i = Emetine hydrochloride intramuscularly daily for six days.

A STUDY ON THE PREPARATION OF AN EFFICIENT EXTRACT OF KURCHI (*HOLARRHENA ANTIDYSENTERICA*)

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THE bark of kurchi (*Holarrhena antidysenterica*) has been spoken of since prehistoric days as an efficient remedy for dysentery. It has been mentioned by Charaka and others in the books of oriental medical science. Lately, the drug has attracted the attention of modern scientists and pharmacologists, so much so that articles regarding the determination of its active principles and its chemistry have been published by no less than a dozen workers within the course of a few years. The therapeutic value of the drug has been found to be due mainly to its contained alkaloids whose actions are as potent as those of emetine, without producing the toxic effect of the latter.

The researches of Acton and Chopra have definitely established that the alkaloids in kurchi have a similar amœbicidal effect to that of emetine. Again, some other workers (Henry and Brown, 1924) hold that conessine, the principal alkaloid of kurchi, alone, like emetine, has less protozoocidal effect *in vitro* than when it is administered in a dilute acid or alkaline medium. They are also of opinion that the efficacy of these and other alkaloids of similar drugs is enhanced when they are administered along with the associated tannins contained in the drugs. They are, however, silent about the effect of the resinous matter in them. This observation of the greater efficacy of the alkaloid when administered with other substances reminds us at once of the applications of many drugs as a whole in our Ayurvedic system. Unfortunately, with the exception of the work of Henry and Brown, which only touches on the subject, there has been to date no scientific investigation on these lines.

The clinical study of the extracts of kurchi, both watery and alcoholic, by A. R. Majumdar (1930) reveals two facts: (1) watery decoctions of kurchi are worthless clinically, and (2) a standardised extract containing a reasonable amount of alkaloids is necessary to get any result in cases of amœbic dysentery. According to him a patient with frequent stools requires 3 to 4 grains of total alkaloids daily. Keeping this in view, in collaboration with the Bengal Chemical and Pharmaceutical Works, he has worked out a process for preparing such an extract containing 1 per cent. $\frac{w}{v}$ of total alkaloids of kurchi. But he has not given the method of preparing this extract in his article. Although Acton and Chopra have reported favourably upon the amœbicidal effect of kurchi-bismuth-iodide, the price of this salt is rather high. Alcoholic extracts of kurchi are both cheaper than any other preparations, and

are handy to administer. But any extract of kurchi will be worthless unless it is standardised.

Having been associated with the analytical side of the medicinal preparations, official, non-official and indigenous, in the Bengal Excise Laboratory under the Public Health Department, the writer has had ample opportunity of testing alcoholic extracts of kurchi produced by the local manufacturers. Real difficulty has been felt in the laboratory when considering the permissibility of granting a licence to manufacture an extract of the same drug at different alcoholic strengths. The necessity of standardising the useful indigenous drugs is thus keenly felt in order to force the manufacturers to put on the market uniform standard preparations. In the absence of standard methods of preparing tinctures and extracts from indigenous drugs, it is very difficult to say which preparation of these drugs is good and which is bad. Taking the concrete example of alcoholic kurchi extract, it has been found that various bazar preparations of this drug are quite different from each other. Some have a low alkaloidal and high tannin and resinous content, while others have a high alkaloidal and low resinous content. The standardisation is thus obviously very necessary. According to Dr. Majumdar (1930), kurchi is so efficacious in cases of amœbic dysentery that it is expected that it will in the near future be included in the British Pharmacopœia. To quote him, 'What preparation will give the maximum effect with the minimum cost is still an open question'; the fact is at once clear that an investigation is necessary into the nature of alcoholic extracts of kurchi (which in the writer's opinion are undoubtedly the cheapest of all preparations) in order to get an idea which of the alcoholic preparations will really be suitable from all points of view. Bearing these points in mind the writer has carried out some experiments in the provincial excise laboratory under the Bengal Public Health Department, the result of which is expected to throw some light on this yet unsolved problem.

EXPERIMENTS

Experiment 1.—Total alkaloid—A sample of kurchi bark supplied through the courtesy of the chemist in charge of Bathgate & Co.'s bonded laboratory was assayed for total alkaloids. The bark was finely powdered and bottled. Ten grammes of this powdered bark were macerated with 6 grammes of slaked lime with a little water and mixed. The whole was then refluxed with benzene and amyl alcohol mixture for 30 minutes and filtered. The residue was further refluxed with a fresh portion of benzene mixture and filtered, and the residue thoroughly washed with the same mixture repeatedly till free from alkaloid. An aliquot portion representing 5 grammes of the bark was exhausted with dilute hydrochloric acid till all the alkaloid was taken up. The alkaloid was

The disease appears to be equally common in men and women in South India. Table II shows the distribution as regards sex among the admissions to the Rayapuram Hospital, for five years. The reputed higher incidence in women has not been met with here.

TABLE II

Sex distribution of granuloma inguinale

Sex	Number of cases	Percentage
Males	27	50.9
Females	26	49.1
TOTAL	53	..

The age distribution of the disease corresponds with the period of maximum sexual activity. The disease is rare in childhood and old age. In two of the cases that occurred in young boys of fifteen the granuloma was around the anus and there was a definite history of sodomy.

TABLE III

Age distribution of granuloma inguinale

Age	Number of cases	Percentage
Between 15-20	4	6.0
" 21-25	13	16.2
" 26-30	21	30.9
" 31-35	12	17.6
" 36-40	13	19.1
" 41-45	5	7.4
Above 46	2	2.8
TOTAL NUMBER OF CASES ..	70	..

The site of the early lesion

Granuloma inguinale has been described as most often met with in the groin. It has often been described on the external aspect of the labia in women. Primary involvement of the mucous membrane of the glans penis has been held to be rare and also a primary involvement of the vaginal wall or cervix. Its venereal origin has been questioned. The involvement of the genitalia has been held to be result of spread of infection from the groin. However, very often a careful analysis of the history will reveal the occurrence of a small sore on the skin or mucosa of the penis, that often heals, and is followed by the development of the granuloma in some part of the genitalia or groin. Very often the history is that of a bubo following a sore. This may have opened of itself or been opened by the surgeon, the granuloma developing at the site of the opening. In other cases the sore on the prepuce persists and gradually passes on into a large granulomatous

ulcer, that involves the shaft of the penis and spreads to the scrotum. Another history that is often obtained is that of a sore that heals and breaks down again, or has been removed by circumcision, the granuloma developing at the line of incision.

TABLE IV

Site of the primary lesion in granuloma inguinale in men

(From a careful analysis of the history of 39 unselected cases admitted into the Venereal Department of the Madras General Hospital during the year 1930.)

Site of the lesion	Number of cases	Percentage
Granuloma following sore on the penis.	29	74.4
Granuloma following bubo ..	8	20.5
Granuloma on circumcision wound.	2	5.1
TOTAL NUMBER STUDIED ..	39	..

A similar analysis could not be made in women since the history was vague.

Thus it becomes apparent that genital infection is possible and does occur in most of the cases in South India. Other modes of infection are possible, since the disease is auto-inoculable. It has been held that prolonged contact is necessary for infection. De Vogel however puts down the incubation period as two weeks. In Guldberg's case the granuloma developed from a bubo which occurred 14 days after as small sore on the penis. While primary lesions are difficult to trace in women, a careful inquiry into the history will often reveal that there has been a sore on the vaginal wall or labia some time before the occurrence of the granuloma. The condition may have been mistaken for a chancre or a soft sore. Extensive ulceration of the vaginal wall may be met with, but this is often late in the disease. Ulceration of the skin round the anus or of the perineum may occur as the very first lesion. Rarely the lower abdominal wall may be the site. If we take into account the analogy with a disease of undoubted venereal origin like syphilis, and the relative frequency of extra-genital chancres, a primary extra-genital lesion in granuloma is just as common. Figure 1 illustrates a case where a granuloma on the lips followed disease on the genitalia. In another case shown to me, an ulcer developed on the cheek following a granuloma on the genitalia. In Donovan's (1905) classical case where the parasite was first described, the granuloma was on the lip following disease of the genitalia. Fox records numerous extra-genital sites such as the nose, cheek, lips, neck, larynx, pharynx, back of hand and thigh. In Thierfelder's (1925) case the

process extended from the external into the middle ear.

The morphology of the lesion.—The earliest lesions that have been noticed, what may be called the primary lesion in granuloma inguinale, are on some part of the genitals. It is about the size of a pea or even smaller. Over this the skin becomes boggy and soft even at the commencement, indicating that the primary infection is through some breach of the surface. This primary sore, as I have called it, is not often diagnosed as granuloma, and very often heals. This early nodule is pink and vascular. Its surface is covered by a thin serous discharge.



Fig. 1.—Inguinal granuloma. Lesion on the lip. There was extensive disease on the genitalia.

Induration is not so marked as in a chancre and the lesion might be mistaken for a soft sore, but the reaction is milder and there is not that angry looking base and raw inflamed edges that are met with in a soft sore. The fully developed granuloma, as distinct from a soft sore, is much more distinctive, in that the surface of the ulcer is raised up above the skin as a nodule with a central mass of granulations. Gradually the inflammatory process spreads and forms an extensive ulcer which often presents the appearance of healing. In women the story is that of a sore on the labia that heals, but the cicatrix breaks down again and forms an intractable ulcer that is extremely chronic. Side by side with lesions on the genitalia, lesions develop on the groin, at the crural angles, and on the skin of the perineum. In any case the striking feature of the ulcer is the new growth of tissue that projects above the surface. This consists of a mass of coarse pink granulations or even nodules that projects above the surface, and shows at the edges a dull bluish appearance from growth of epithelium. The mass is

soft and very vascular, the granulations varying in size from a pin's head to coarse nodules of the size of a pea or bean. The edges are always raised, crenated and wavy, gradually extending in places while other areas show definite healing. The condition is extremely chronic and indolent, the ulcer continuing to spread for months or even years. The cicatrization may be on one side or more irregular, the cicatrix often breaking down in the centre discharging a thin serous fluid. In many cases the infection may spread to contiguous surfaces, probably by auto-inoculation; but even apart from this, fresh foci in the shape of small nodules quite commonly may be met with in the neighbouring skin. In other cases, these nodules are small abscesses containing granular purulent material. Sometimes tumour-like nodules may communicate with cavities and may continue to discharge thin sero-purulent material, and the condition may clinically resemble mycetoma. On the other hand, extensive scabbing may be present at the edge of the ulcer, particularly when secondary infections with pyogenic cocci are present.

The process spreads in an annular fashion especially in the groin. It may encircle the genitalia extending across the mons and behind to the perineum. On the genitalia extension may occur in any direction, but more commonly the folds of integument such as the peno-scrotal angle, or the outer or inner edge of the labia may be affected. Dense cicatrization may occur with healing, giving rise to extreme deformity, hence the name 'sclerosing granuloma'. In women the urethral canal may be involved and the meatus may be converted into a wide irregular opening with thick sclerosed edges (see figure 2). Sometimes large polypoid masses

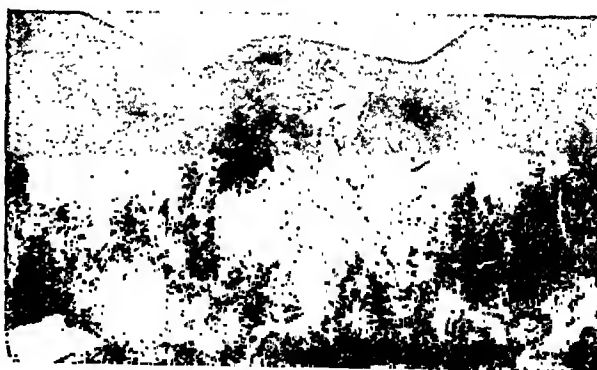


Fig. 2.—Cicatrization following granuloma inguinale, with involvement of the urethral canal.

may project from the urethral canal and the condition may be mistaken for caruncle. Involvement of the cervix is not usual. A common feature met with in women, and due to obstruction of the deep lymphatics of the skin of the genitalia, is a solid oedema of the vulva with a thickening of the skin. In other cases the obstruction may be more irregular, and

nodular polypoid grape-like masses of hypertrophied skin may project from the labia with cicatrising ulcers on the outer side, a condition that may resemble elephantiasis (see figure 3). A true non-filarial elephantiasis of the



Fig. 3.—Polypoid masses projecting from the vulva; pseudo-elephantoid condition due to granuloma inguinale.

vulva may occur and the mass may be so large as to require removal. Spread may occur along the inner side of the thigh as low down as the knee.

As has already been mentioned, extra-genital infection with granuloma is rare, but occasionally cases may be met with in the axilla and the lower abdominal wall, and they may be mistaken for lupus. Ulceration round the anus is quite common without lesions on the genitalia. This may be followed by sclerosis with stricture of the anal canal. These cases are much more resistant to treatment, they frequently heal up and break down again. Other extra-genital sites of infection, such as the lips and cheeks, are mere associated lesions.

TABLE V

Site of the well-developed lesion in men and women

Site of the lesion	Number of cases	Percentage
External genitalia ..	28	44.4
Inguinal region ..	6	9.5
External genitalia and inguinal region.	16	25.4
Perineum ..	3	4.8
External genitalia and perineum.	3	4.8
Skin round anus ..	5	8.0
Lower abdominal wall ..	1	1.6
Lip ..	1	1.6
TOTAL CASES STUDIED ..	63	..

Enlargement of the lymphatic glands is not well defined or distinctive when the lesion is well developed, though it occurs to a slight extent in about 40 per cent. of cases. It is,

however, premature to decide whether a lymphadenitis occurs in all cases during what I have called the primary stage of the disease. That such lymphadenitis does occur in some of the cases is evident from the history of bubo that is often met with. In some cases even late in the disease, an acute septic lymphadenitis does occur followed by suppuration.

TABLE VI

Enlargement of the lymphatic glands of the groin in 39 cases of granuloma inguinale

Type of enlargement	Number of cases	Percentage
Well-defined enlargement ..	9	23.1
Slight enlargement ..	7	18.0

Visceralisation has been described by Thierfelder and a case of abscess of the liver has been recorded. So far no such cases have been met with in Madras, though it is difficult to say how far the internal organs are affected in those cases which terminate in chronic cachexia. Chronic cystitis may occasionally be met with in women. In cases with extensive disease of the perineum the process seems to spread up to and involve the rectum and surrounding tissues, and very often death occurs from cachexia with a low type of fever. Spontaneous cure may be met with rarely, but occasionally cases occur where a cure has been effected by the application of caustics. Syphilis may co-exist and complicate the clinical picture, but the serum reactions are distinctive. A well-defined positive Wassermann reaction is never met with in granuloma inguinale unless syphilis co-exists.

The histology of the lesion

A study of the early nodules that are met with, shows two distinctive features. There is in the main a desquamation of the superficial layers of the epidermis so that the keratinised layers are lost. Together with this there is a cell infiltration of the corium in the papillae just below the germinal layer. The deeper layers of the epidermis show a tendency to become spread out owing to a swelling of the intercellular material. Over the ulcerated area these layers are cast off, but proliferation occurs in the neighbourhood, so that the normal papillary folds are exaggerated and down growths of epithelium are prominent (see figure 4). The denuded area presents the appearance of acute inflammation. Emigration of leucocytes forms a prominent feature, but exudation and fibrin formation are scanty. The type of cell reaction on the surface is mostly polymorphonuclear, but mononuclears are present in numbers. Just below the surface is granulation tissue containing numerous endothelial cells and fibroblasts arranged around embryonic

capillary loops. Superficial necrosis of tissue is not well marked. In the swollen endothelium of the newly-formed solid capillary buds, and in the mononuclear wandering cells, clumps of coccoid and cocco-bacillary bodies may occasionally be made out.



Fig. 4.—Inguinal granuloma ($\times 125$ approximately) showing an early nodule under the epidermis. Note the atrophy of the epithelium over the nodule and the proliferation in the neighbourhood.

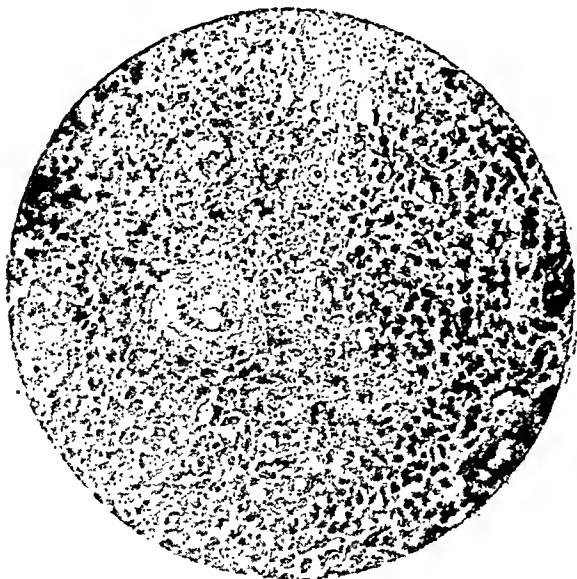


Fig. 5.—Inguinal granuloma ($\times 750$ approximately) showing the embryonic capillary buds surrounded by lymphocytes and proliferating endothelium.

While this is the type of reaction that is present on the surface, the deeper layers show evidences of chronic inflammation in the

well-developed granuloma. Polymorphonuclear leucocytes are not so numerous, but accumulations of lymphocytes and plasma cells are marked, especially round the small blood vessels, a feature that is quite like the reaction that is met with in syphilis (see figure 5). Endarteritis obliterans, however, is not a feature in this series of cases. Proliferation of fibroblasts is quite well marked in the deeper layers. In old cases, there are dense strands of fibrous tissue with here and there collections of plasma cells and lymphocytes in the crevices of tissue and around small capillaries. Giant-cell formation is not met with and caseation necrosis does not occur. The epithelium in the neighbourhood shows a loss of the keratinised layers. The whole histological picture is distinctive and resembles to some extent the reaction in the primary sore of syphilis. Manson-Bahr (1929) notices a resemblance to the morphology of rhinoscleroma, but this is more apparent than real, since the nodules of rhinoscleroma seldom ulcerate and the histologic reaction is sufficiently distinctive, the characteristic feature being the presence of the large cells of Mikulicz—the rhinoscleroma cells—which are not met with in granuloma.

Discussion

The primary lesion in granuloma has been overlooked. The infection has been believed to be through some breach of surface, but the history of a definite primary sore, that is often met with, has not been emphasised. The reputed common incidence on the groin has been looked upon as indicating a non-venereal origin, since definite venereal lesions would mostly be on the genitalia. The name inguinal granuloma itself lays stress on the occurrence of lesions in the groin. The condition has been even looked upon as a primary disease of the skin of the groin, occurring by inoculation of abraded areas in the tropics, where lesions caused by fungi are quite common in and about the inguinal region. Sexual contact, according to this view, is only one of the modes of infection. The difficulty in experimental reproduction of the disease, its sparse incidence and race distribution have been put forward as against a venereal origin.

The present study emphasises that the main incidence of the disease is on the genitalia and not on the groin. The condition is met with at the period of life associated with the greatest sexual activity. The primary lesion is a sore that most often heals over, and is most commonly found in the genitalia. Whether this primary lesion is a separate factor and merely serves as a means for the entrance of the infective agent of the granuloma is yet uncertain; but the tendency to healing side by side with ulceration and the primary sore which often heals and breaks down again are features of

granulomata. That the infection is one that does not readily 'catch' is evident. The curious incidence of granuloma on a circumcision wound and at the side of a bubo that has been opened, indicates that the infective agent is present in the tissues in and about the genitalia. This also points to the existence of a previous stage, when the virus gains an entrance into the tissues. With regard to the mode of infection there are thus only two possibilities. The primary sore may be caused by one phase of the infective agent which lies dormant or undergoes multiplication in the tissues; or it may be that the granuloma is of the nature of a secondary infection, the primary sore being of different origin. The existence of lymphadenitis has been denied; but that it does occur in a fair proportion of cases is evident from table VI. That a lymphatic involvement may occur in the early stage of the disease is probable, from the frequency of the disease in the groin following on lesions on the genitalia.

Thus a study of the site of the lesion in granuloma inguinale and its mode of commencement indicate that the condition is most often met with in the genitalia, and that it is of venereal origin.

The term venereal granuloma would thus be more suitable, as indicating the real nature of the condition.

Acknowledgments

Some of the cases cited above were under the care of Mr. R. V. Rajam, M.S., M.R.C.P.E., Venereal Surgeon, General Hospital, Madras, and the others were under the care of Mr. C. R. Krishnasamy, M.B., C.M., Honorary Venereal Surgeon, Government Rayapuram Hospital, Madras. The writer has great pleasure in acknowledging their kindness in allowing him to examine some of their cases and study their records. He is also greatly indebted to Dr. Stephanos, the lady doctor in charge of the women's section of the out-patient department of the Rayapuram Hospital, for her kind co-operation in the study of some of the cases. To Dr. A. S. Annamalai and Dr. S. Krishnasamy of the Pathology Department of this hospital the writer is equally indebted for assistance in compiling the records of cases cited.

REFERENCES

- De Vogel, M. W. T. (1928). *Bull. Soc. Path. Exot.*, Tome XXI, p. 354.
- Donovan, C. (1905). *Indian Med. Gaz.*, Vol. XL, p. 414.
- Fox, H. (1926). *Journ. Amer. Med. Assoc.*, Vol. LXXXVII, p. 1785.
- Manson-Bahr, P. H. (1929). *Manson's Tropical Diseases*. London: Cassell & Company, Ltd.
- Thierfelder, M. U. (1925). *Arch. Schiffs- u. Trop.-Hyg.*, Band XXIX, p. 690.

RABIES IN THE MONGOOSE

FURTHER OBSERVATIONS

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I. Reports from records

SINCE the last communication was sent (Grevall, 1932) information has been received about seven more cases of mongoose bite, one at Lahore, another at Lucknow, and five at Kasauli. The following Kasauli cases are worth recording:—

1. Case No. 4791 of 1932

J. S., aged 'about' 50 (more probably 60), male, of S. J., near Chhajli, near Sanam, Patiala State. Bitten on 1st August, 1932. Came for treatment on 3rd August, 1932. Finished treatment on 17th August, 1932. He stated:—

'I was sitting outside my house when a mongoose rushed at me and caught hold of my finger tip. A few boys of the village came running after it saying that it was mad and had bitten a dog and a grown-up calf in the village. The mongoose, however, escaped into an enclosure where farmers stack dry sticks and fuel of similar nature.

In detaching the mongoose I had to roll it over and discovered that it was a male. It was seen again the same evening and is still at large. The women and children are avoiding that part of the village.

The village is a small one and consists of about 100 houses surrounded by fields.

The wound bled profusely for some time after the bite.

At Borah, in Nabha State, at a distance of some 17 to 18 kos from my village, two years ago, a man was bitten by a mongoose. He did not undergo any anti-rabic treatment and died, 10 to 15 days after the bite, from hydrophobia. He had to be chained up for two days before he died.

Last year two patients from my village were treated at Kasauli for jackal bite.'

(Translated from Punjabi by S. D. S. G.)

2. Case No. 5001 of 1932

P., aged 7½, male, of J. G., district Kangra. Bitten 10th August, 1932. Brought for treatment on 14th August, 1932. Finished treatment on 27th August, 1932. His father stated:—

'The boy was playing in a room in the house when a mongoose came in, bit the boy on the face without provocation and ran away. Next day the mongoose bit another boy outside his house about a furlong from our house. It was then chased and killed.

Besides the two boys the animal had attacked two men who avoided being bitten.

The animal was uttering the sound of *khen khen khen* and was not afraid of even a crowd.

I have known mongooses to be mad before. It is a common knowledge in my part of the country that cattle bitten by them die. I have brought the boy for treatment because of the bite on the face. For serious bites I have no faith in indigenous medicines for rabies. The other boy was bitten on the hand.* He is being treated in the village by indigenous medicines.

The wounds were cauterised next day. A swelling on the face had been noticed the previous evening.'

(Translated from Hindi by S. D. S. G.)

* The seriousness of a bite on the fingers was pointed out to the patient.

3. Case No. 5077 of 1932

H. R., aged 22, a Patwari at IX, tahsil K. P., district Sri Ganga Nagar, canal area. Bitten 4th August, 1932. Came for treatment on 17th August, 1932. Finished treatment on 30th August, 1932. He stated:—

'I was sleeping, in the rest house, on a *charpai*, when I heard the sound of *cur cur cur*. A little later a mongoose caught hold of one of my fingers. I jerked the animal off and in doing so banged it against the edge of the *charpai*. I also called out for help and obtained a stick. I had hardly pointed the stick at the animal when it jumped at me but caught hold of the edge of the *charpai* instead. It also attacked two more men who had come in but did not succeed in inflicting a bite. One of these men hit it with a heavy stick and threw it out of the room where it died in a convulsion.

The animal was a female but had no litter teats (small and dry).

In the same bungalow, the previous night, another man was also bitten by what he had thought to be a snake. His wounds were cauterised.

My father is a *hakim*. He consulted the *Tib-i-Akbar* and found that mongooses suffer from rabies like dogs. He gave me onion water to drink and also onion pulp in food. I also attended a hospital at K. but was advised to go to Ganga Nagar. The doctor at Ganga Nagar wrote to Kasauli with the result that I am here.'

(Translated from Urdu by S. D. S. G.)

4. Case No. 6313 of 1932

B. S., aged 6, male, of L., district Karnal. Bitten 27th October, 1932. Brought for treatment on 29th October, 1932. Still under treatment (on 10th November, 1932). His father states:—

'The boy was seated in an open-air class of a village school when a mongoose rushed in amongst the class and bit him on the lip. The boy beat off the animal with his cap. It then attacked another boy (the next case). The animal was then killed. I have not heard of mongooses attacking unprovoked before.

The village consists of about 50 houses. The school has a hedge round it.'

5. Case No. 6341 of 1932

J., aged 9, male, of L., district Karnal. Bitten on 27th October, 1932. Brought for treatment on 29th October, 1932. Still under treatment (on 10th November, 1932). This is the other boy referred to above. He was also bitten on the face.

These cases together with the cases given in the previous communication total eight bitten by seven mongooses in seven different localities. Adding to them the two cases from Lahore and Lucknow and the mongoose proved rabid microscopically (previous communication) there have been reported ten cases of mongoose bites and ten biting mongooses, in ten different localities, during the last seven months.

Further information has also been received about the girl bitten badly, on 3rd May, 1932, by a rabid mongoose and not treated by modern methods (items 1 and 2 of the last communication) and also about the position of true rabies in South Africa where its existence appears to have been doubted.

Copy of a letter from G. S. V. A., dated B., district Jullundur, 13th October, 1932. Receipt No. 9902 of 1932.

'Dear Sir,—The girl bitten by the mongoose is quite all right. There is no complaint of any kind. This statement is submitted as an information.

—G. S. V. A.'

(Translated by S. D. S. G. from Urdu.)

Copy of a letter from the South African Institute for Medical Research, Hospital Street, Johannesburg, dated 12th July, 1932.

'Dear Sir,—The existence of rabies in South Africa has recently been established.

In this connection we are desirous of carrying out experimental work to ascertain whether local strains of the virus are similar to those of overseas origin. For this purpose we should be very grateful if you would be good enough to let us have small portions of glycerinated brain or cord tissue representing—(a) street virus, (b) fixed virus, obtained from cases of rabies in your district.

Details of the origin, virulence, etc., of the specimens as well as any information relative to differences in strain of rabies virus that you have encountered would be very highly appreciated.—I remain,

Yours faithfully,
S. L.,
Director.'

II. Comments and speculation

In all the five cases described above we are, evidently, dealing with rabid mongooses. The localities are instances of small human habitations surrounded by vegetation thick enough to offer an habitat to a wild carnivore, the mongoose. A direct introduction of rabies by the wild carnivore without the intermediation of the domestic carnivore, the dog, is being observed. The fact seems to be fairly well known to farmers from observations on man and cattle.

The question arises whether the virus in the wild carnivores is more virulent or less so than in the dog. The girl 'bitten badly' by a rabid mongoose (proved microscopically) and not treated by modern methods has not died. On the other hand a man is said to have died in 10 to 15 days after a mongoose bite. Similar differences in the infectivity of rabid dogs are well known. The rabid mongooses appear to have been more active and energetic than rabid dogs usually are. Do the wild carnivores stand the disease better than the dogs and sometimes get over it? Is there a definite chronic state of the disease to be found amongst them? Both these occurrences have been recorded as rarities in rabbits infected with fixed virus under experimental conditions (Remlinger, 1919) and in dogs infected with street virus under natural conditions (Marie, 1927). Are these occurrences common amongst the wild carnivores which live under more natural conditions than the domestic carnivores? The *phonhin* (or female jackal with a litter) believed by the farmers in this part of the Punjab to be the primary vector of rabies is heard in the villages for weeks together at nights. Biologically it is not in the best interests of a parasite (which presumably the virus of rabies is) to be always lethal in infection, as by being so it is likely to exhaust its nidus and thus exterminate itself.

The letter from South Africa defines the position of rabies in that country. The disease appears to be true rabies in spite of the 'fact

that it has been confined to the wild carnivores (of the family Viveridæ) ' (McKendrick, 1931).

Does the disease, then, smoulder in the forests and flare up in inhabited areas because of the greater liability and susceptibility of the dog when compared to the wild carnivores? Does the apparent stamping out of the disease mean an extinguishing of the flaring only and not of the smouldering? The facts recorded in this and the previous communication appear to favour this view.

Summary

1. Five cases of mongoose bite treated at Kasauli have been described. Adding to them the cases previously described, the cases treated at the centres served from Kasauli and a mongoose brain examined at Kasauli, there have been reported ten cases of mongoose bite and ten biting mongooses, in ten different localities, during the last seven months.

2. A note is made of the fact that the existence of rabies in South Africa has recently been established in spite of the fact that the dog is not the usual vector.

3. The suggestion made in the previous communication that rabies may be essentially a disease of jungles is repeated. A further suggestion is made that the disease may not be always fatal in jungles, amongst the wild carnivores.

REFERENCES

- Greal, S. D. S. (1932). Rabies in the Mongoose. *Indian Med. Gaz.*, Vol. LXVII, p. 451.
 Marie, A. C. (1927). *League of Nations Reports*, C. H. 531 (i), p. 17.
 McKendrick, A. G. (1931). Rabies. A Review of Recent Articles. *Trop. Dis. Bull.*, Vol. XXVIII, p. 741.
 Remlinger, P. (1919). A Case of Spontaneous Recovery in the Rabbit following upon Sub-dural Inoculation with Fixed Virus. Abstract in *Trop. Vet. Bull.*, Vol. VII, p. 243.

AN EASY METHOD FOR ESTIMATING THE PROTEIN CONTENT OF MILK

By B. B. BRAHMACHARI, D.P.H.

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IN the routine analyses of milk under the Food Adulteration Act, we find the specific gravity, fat and total solids, and our work is done. But the profession as well as the public may like to know the quantities of the other nutrients in the milk. Milk proteins are of as much importance from the biological point of view as the milk fat; if the latter contains the vitamins, the former contains the amino-acids which are essential for growth. The Kjeldahl process, the usual method for estimating the proteins, is not very suitable for routine work; they can be estimated fairly easily from the aldehyde figures by formol-titration methods, such as those of Steinegger or of Richmond and Miller. But the method which is the subject of

this paper is similar to the one for estimating albumen in the urine by precipitating it with a reagent, it is exceedingly easy, and can be done by any medical man.

We have many precipitants for proteins, and just as in the case of urine we get a fairly workable idea of the amount of albumen from the depth of the precipitate, so in the case of milk there is no reason why a method on the same lines should not be equally useful. In phosphotungstic acid we have a suitable precipitant for milk, especially in the form of Bogg's reagent as given by Kolmer and Boerner (1925), viz,

- | | |
|------------------------------------|--------------|
| (1) Phosphotungstic acid | .. 25 gm. |
| Distilled water | .. 125 c.cm. |
| (2) Concentrated hydrochloric acid | .. 25 c.cm. |
| Distilled water | .. 100 c.cm. |

After the phosphotungstic acid is completely dissolved, the two solutions are mixed and kept in a dark glass bottle. The process of analysis consists of—

- (1) Diluting the milk 1:20 with distilled water.
- (2) Filling an Eshach tube to mark U.
- (3) Adding Bogg's reagent to mark R and inverting several times.
- (4) Setting aside for 24 hours.
- (5) Reading off directly on the scale and multiplying by 2.

I have tried this method on samples of cow and buffalo milk, 10 of each, analysing them also by the Kjeldahl process. The result is given on the next page.

The differences between corresponding figures of the two columns are not significant.

Madras has standardised milk protein as one of the constants under the Madras Food Adulteration Act, 1918 (by Notification II, Order No. 1329-P.H., dated the 4th August, 1926), fixing it at not less than 0.5 per cent. of nitrogen for cow milk and 0.53 per cent. for buffalo milk which are 3.19 and 3.38 per cent. respectively as milk proteins. Stewart and Chatterjee (1931) found that this standard agreed with the result they obtained on 15 samples of milk, fresh and after souring. We have analysed up to date 46 samples of genuine cow's milk and 25 of buffalo milk, each drawn from a separate animal, using the Kjeldahl process for proteins, and multiplying the figures for nitrogen into 6.38; 9 out of our 46 samples of the cow milk and 6 out of the 25 samples of buffalo milk gave figures which are below the Madras standards, but the departures are no greater than those of milk fat in the genuine samples from its legal standards; so the protein may very well be utilised as a supplementary constant; if so, the simple method described above,

(Continued at foot of next page)

COMPARATIVE NOTES ON THE
CRYOSCOPY OF MILK

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It is well known that osmosis is of fundamental importance in the general metabolism of animal life. The direct measurement of osmotic pressure, however, is a matter of considerable difficulty, and it is more convenient to measure other properties of solutions of known relationship to the osmotic pressure. The depression of freezing point or cryoscopic determination is the most accurate and commonly employed method.

In a case of mammals, milk is the natural fluid for rearing the young, and a study of its cryoscopy is not without interest. Now the osmotic pressure of a given sample of milk is mainly due to the soluble salts and lactose or milk-sugar which it contains. The influence of the fat (the most variable constituent) and the proteins is practically negligible. A certain constancy of the freezing point may therefore be anticipated. Although a number of papers already published on cow's milk substantiate the truth of this statement, references to other mammals of importance are inadequate, and an attempt has been made to supply some necessary data in this investigation.

Only authentic samples from individuals of four different mammals were studied, each accounting for a series of 30 examinations. In

the case of human milk it is important to note that the specimens were drawn 5 to 10 days after parturition, and that both mother and infant were progressing satisfactorily.

A cryoscope of the Beckmann type was employed, the accessories being readily available. Application of correction factors was avoided by a carefully standardised procedure, and no samples showed an abnormal acidity, so that errors were obviated in this respect.

In carrying out the test, the apparatus was filled with a mixture of crushed ice and salt to serve as a freezing medium. A sufficient quantity of the sample (previously cooled) to completely immerse the thermometer bulb was introduced into the freezing tube. The thermometer and stirrer were then inserted. Stirring was maintained uniformly at a rate of about once per second, and the temperature of the cooling bath adjusted, so that a supercooling of the sample between 1.0° and 1.5°C. was readily obtained. The mercury rose rapidly to its highest point when the reading was taken after tapping the upper end of the thermometer two or three times.

The zero point of the thermometer was ascertained by observing the freezing point of recently boiled and cooled distilled water under similar conditions. This point was periodically checked for each new set of determinations.

Tables I, II, III, and IV, give the results and descriptive details, together with the analytical figures relating to the chemical composition of the samples.

(Continued from previous page)

PROTEIN IN MILK

*Estimated by Kjeldahl's method and by precipitation with phosphotungstic acid in an
Eshach's tube*

COW MILK			BUFFALO MILK		
Number	By Kjeldahl's method	By precipitation in Eshach's tube	Number	By Kjeldahl's method	By precipitation in Eshach's tube
1	3.46	3.4	1	3.83	4.0
2	2.96	2.8	2	3.45	3.6
3	3.69	3.8	3	4.59	4.0
4	2.14	2.2	4	4.65	4.6
5	3.53	3.6	5	3.31	3.6
6	3.59	3.5	6	3.25	3.4
7	3.39	3.4	7	3.83	4.0
8	3.02	3.0	8	3.64	3.8
9	3.19	3.0	9	3.83	4.0
10	3.5	3.6	10	3.76	4.0

giving practically the same result as the Kjeldahl process, will be a help even in the analysis of milk for detection of adulteration.

In conclusion, I acknowledge my indebtedness to my assistant Mr. S. K. Banerjee for helping me in the analysis of all the samples in the paper and for the keen interest he has been taking in my research on milk.

REFERENCES

- Kolmer, J. A., and Boerner, F. (1925). *Laboratory Diagnostic Methods*, p. 113. New York: D. Appleton and Company.
 Richmond, H. D. (1920). *Dairy Chemistry*, p. 182. London: Charles Griffin & Co., Ltd.
 Stewart, A. D., and Chatterjee, N. K. (1931). Notes on the Determination of the Nitrogen in Sour Milk as a Subsidiary Standard of Purity. *Indian Med. Gaz.*, Vol. LXVI, p. 320.

TABLE I
Buffalo's milk

Number	Fat, per cent.	Solids-not-fat, per cent.	Total solids, per cent.	Depression of freezing point, °C.	* Acidity
1	6.40	9.90	16.30	0.575	1.1
2	5.51	9.69	15.20	0.570	0.9
3	6.82	10.10	16.92	0.580	1.3
4	7.83	9.77	17.60	0.575	1.3
5	5.70	9.45	15.15	0.570	1.6
6	9.22	10.00	19.22	0.575	1.2
7	7.90	9.50	17.40	0.575	1.1
8	6.68	9.37	16.05	0.565	1.5
9	8.82	10.01	18.83	0.590	1.4
10	5.79	9.57	15.36	0.575	1.6
11	9.09	10.35	19.44	0.585	1.3
12	5.02	10.20	15.22	0.580	1.3
13	5.10	10.41	15.51	0.590	1.3
14	6.40	9.60	16.00	0.575	0.8
15	8.41	9.24	17.65	0.560	0.8
16	6.02	9.88	15.90	0.570	1.0
17	7.22	9.38	16.60	0.560	1.5
18	9.20	10.21	19.41	0.590	1.2
19	8.35	9.25	17.60	0.570	1.1
20	9.50	9.88	19.38	0.575	1.7
21	7.61	10.30	17.91	0.590	1.3
22	7.51	10.00	17.51	0.580	1.3
23	7.92	9.93	17.85	0.585	1.7
24	8.53	9.62	18.15	0.575	1.3
25	7.41	9.82	17.23	0.580	1.2
26	5.68	9.21	14.89	0.560	1.5
27	8.59	10.10	18.69	0.580	1.4
28	10.00	10.72	20.72	0.590	1.1
29	6.80	9.74	16.54	0.570	1.0
30	5.21	9.11	14.32	0.560	1.5

TABLE II
Cow's milk

Number	Fat, per cent.	Solids-not-fat, per cent.	Total solids, per cent.	Depression of freezing point, °C.	* Acidity
1	4.90	8.74	13.64	0.560.	1.2
2	5.02	9.40	14.42	0.580	1.9
3	4.39	8.81	13.20	0.565	1.7
4	3.10	8.75	11.85	0.570	1.7
5	5.20	8.82	14.02	0.560	1.5
6	5.02	8.91	13.93	0.560	1.4
7	4.10	8.70	12.80	0.555	1.5
8	4.65	8.85	13.50	0.570	2.0
9	3.09	8.91	12.00	0.570	1.4
10	4.78	9.10	13.88	0.575	1.9
11	3.80	9.80	13.60	0.580	1.5
12	4.85	9.44	14.29	0.575	1.6
13	4.71	9.12	13.83	0.570	1.6
14	3.50	8.90	12.40	0.570	1.6
15	4.01	9.15	13.16	0.570	1.2
16	4.85	9.46	14.31	0.575	1.6
17	3.05	8.96	12.01	0.560	1.7
18	5.03	8.81	13.84	0.550	1.4
19	6.50	9.40	15.90	0.580	1.5
20	3.83	9.31	13.14	0.570	1.7
21	4.31	8.80	13.11	0.555	1.4
22	5.40	9.02	14.42	0.560	1.5
23	4.10	8.88	12.98	0.550	1.5
24	4.45	8.87	13.32	0.565	2.1
25	4.41	8.75	13.16	0.560	2.2
26	4.62	9.10	13.72	0.575	2.0
27	3.60	8.70	12.30	0.550	1.6
28	5.79	9.23	15.02	0.570	1.7
29	4.12	9.28	13.40	0.570	1.7
30	5.94	9.45	15.39	0.575	1.2

* Number of c.cm. of N/10 sodium hydroxide solution per 10 c.cm. of milk.

TABLE III
Goat's milk

Number	Fat, per cent.	Solids-not-fat, per cent.	Total solids, per cent.	Depression of freezing point, °C.	* Acidity
1	5.75	8.83	14.58	0.550	1.6
2	6.75	9.78	16.53	0.565	1.9
3	3.49	9.79	13.28	0.570	1.6
4	2.02	10.17	12.19	0.580	1.5
5	3.20	9.29	12.49	0.560	2.2
6	2.58	10.03	12.61	0.590	1.6
7	1.90	10.18	12.08	0.590	1.8
8	2.71	10.42	13.13	0.590	1.7
9	4.77	10.07	14.84	0.580	1.5
10	2.03	10.26	12.29	0.575	1.4
11	4.62	10.48	15.10	0.580	1.9
12	4.50	10.69	15.19	0.585	1.3
13	3.75	10.46	14.21	0.585	1.2
14	4.60	9.57	14.17	0.575	1.6
15	3.29	9.85	13.14	0.580	1.5
16	2.56	10.21	12.77	0.580	1.3
17	6.09	9.42	15.51	0.580	2.1
18	2.48	9.68	12.16	0.585	1.5
19	4.26	9.72	13.98	0.580	1.5
20	6.22	9.46	15.68	0.575	1.9
21	3.45	9.25	12.70	0.565	1.4
22	5.44	9.56	15.00	0.580	1.3
23	5.42	9.69	15.11	0.585	2.1
24	3.08	9.92	13.00	0.585	1.6
25	3.51	10.10	13.61	0.585	1.6
26	3.76	9.89	13.65	0.580	1.2
27	6.20	9.75	15.95	0.580	1.8
28	2.43	9.66	12.09	0.575	1.2
29	6.71	10.42	17.13	0.585	1.3
30	1.70	9.80	11.50	0.580	0.8

TABLE IV
Human milk

Number	Nationality	Fat, per cent.	Solids-not-fat, per cent.	Total solids, per cent.	Depression of freezing point, °C.	* Acidity
1	Anglo-Indian ..	4.71	9.75	14.46	0.585	0.3
2	Do. ..	3.30	9.90	13.20	0.580	0.3
3	Burmese ..	4.42	8.91	13.33	0.575	1.1
4	Do. ..	4.47	8.93	13.40	0.585	1.3
5	Do. ..	4.22	9.44	13.66	0.580	1.2
6	Do. ..	3.78	9.74	13.52	0.590	0.2
7	Do. ..	5.29	9.15	14.44	0.585	1.5
8	Do. ..	3.91	8.96	12.87	0.570	0.4
9	Do. ..	3.30	8.81	12.11	0.570	0.3
10	Do. ..	3.69	8.50	12.19	0.555	0.8
11	Chinese ..	3.75	9.70	13.45	0.575	0.7
12	Do. ..	5.32	9.31	14.63	0.590	0.2
13	Do. ..	3.93	9.12	13.05	0.590	1.3
14	Do. ..	5.13	8.76	13.89	0.550	0.2
15	Do. ..	4.04	8.66	12.70	0.560	0.8
16	Do. ..	5.44	8.87	14.31	0.565	0.5
17	Do. ..	6.30	8.82	15.12	0.570	0.6
18	Do. ..	3.10	8.75	11.85	0.565	0.8
19	Indian ..	3.80	8.07	11.87	0.550	1.6
20	Do. ..	4.63	8.97	13.60	0.585	0.8
21	Do. ..	5.11	9.15	14.26	0.590	0.4
22	Do. ..	6.29	9.15	15.44	0.585	0.5
23	Do. ..	3.86	9.00	12.86	0.565	0.3
24	Do. ..	6.12	8.90	15.02	0.580	0.6
25	Do. ..	5.02	9.78	14.80	0.585	1.5
26	Do. ..	4.40	9.60	14.00	0.585	1.1
27	Do. ..	3.72	9.06	12.78	0.580	0.4
28	Do. ..	6.70	8.66	15.36	0.570	0.4
29	Do. ..	5.61	8.92	14.53	0.570	0.6
30	Do. ..	3.52	8.80	12.32	0.570	0.8

* Number of c.cm. of N/10 sodium hydroxide solution per 10 c.cm. of milk.

TABLE V

				FAT, PER CENT.		SOLIDS-NOT-FAT, PER CENT.		* DEPRESSION OF FREEZING POINT, °C.	
				Min.	Max.	Min.	Max.	Min.	Max.
Buffalo	5.02	10.00	9.11	10.72	0.560	0.590
Cow	3.05	6.50	8.70	9.80	0.550	0.580
Goat	1.70	6.75	8.83	10.69	0.550	0.590
Woman	3.10	6.70	8.07	9.90	0.550	0.590

*The 'depression of freezing point' is given in preference to the 'freezing point' in order to eliminate the minus sign.

The figures for solids-not-fat varied considerably in each series, and the fat results showed enormous variation, particularly in the case of goat's milk, where the maximum was four times the minimum. Only the freezing-point figures approached constancy. These facts are brought out clearly in table V.

The results not only demonstrate the constancy of the freezing point within each series, but an extraordinary similarity between one series and another is shown. Human milk is worthy of special notice as it contains a relatively higher percentage of milk-sugar than that of the other mammals under consideration. The quantity of soluble salts present, however, is considerably lower. It would appear, therefore, that the sum effect of these two factors is similar in all four cases, and that the freezing point exhibits a comparatively small range of values.

Dried milk and infant foods

One sample of dried milk (powdered whole milk), and three samples of infant food derived from dried milk were recently received in the laboratory. The former was prepared for use according to the instructions provided (*i.e.*, to regenerate the original milk), and the latter were prepared for feeding as directed for the first week. The usual analysis was extended so as to include the cryoscopic determination as a matter of interest.

The approximate composition of the resulting preparations and the values obtained by the

eryoscopic test are indicated in table VI below :—

TABLE VI

	Dried milk	INFANT FOODS		
		No. 1	No. 2	No. 3
Fat ..	3.6	2.0	1.8	1.0
Proteins ..	3.2	2.9	2.4	0.9
Sugar ..	4.7	5.1	5.0	1.8
Mineral matter	0.7	0.7	0.5	0.2
Water ..	87.8	89.3	90.3	96.1
	100.0	100.0	100.0	100.0
Depression of freezing point, °C.	0.580	0.575	0.515	0.195

The extraordinary degree of dilution recommended for 'No. 3' accounts for its relative deficiency in almost all of the constituents and the low depression of freezing point.

[*Note.*—The attention of readers is drawn to a paper published in the *Indian Journ. Med. Res.*, Vol. XVIII, p. 57, on 'The Cryoscopy of Calcutta Milk' by Lieut.-Col. A. D. Stewart and Mr. N. L. Banerjea, of the Calcutta School of Tropical Medicine and Hygiene, who carried out a similar series of cryoscopic estimations. —EDITOR, *I. M. G.*]

A Mirror of Hospital Practice

CYANOSIS AFTER PLASMOCHIN

By R. N. CHOPRA, M.A., M.D. (Cantab.)
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and

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MR. T. E. M., aged 28, European male, was admitted into the Carmichael Hospital for Tropical Diseases on 12th September, 1932, with the following complaints :—

- (1) Cyanosis all over the body.
- (2) Pain in the epigastric region and in the neck.

History.—During the past six weeks the patient had several attacks of malaria. Although no microscopical examination of the blood for malarial parasites was made at that time, the clinical symptoms of rigor and sweating, together with the improvement following the administration of quinine, pointed to a plasmodium infection. The last attack was from 26th August to 2nd September. The fever used to come every alternate day; it was attended with rigors, and subsided with sweating. Treatment outside the hospital was started by his doctor on 30th August; he was given, in all, 53 grains of quinine by the mouth as well as two injections of quinine bihydrochloride, ten grains each, on 30th August and 1st September. The temperature came down to normal on 3rd September and he was ordered to take two tablets of plasmochin (0.01 gramme

each) thrice daily for five consecutive days. He took four tablets on 4th September, six tablets on each of the next four days, and two tablets on 9th September, thus making up a total of thirty tablets or 0.3 gramme of plasmochin.

The patient first noticed he was getting 'blue all over his body' on 6th September, but he thought nothing of it. On 9th September he became very blue, was dyspnoeic, and felt very weak and prostrated. He was getting cold sweats on the forehead, and severe pain in the epigastric region, in the neck and along the back. He had no appetite and was constipated. The drug was discontinued on 9th September, and he felt slightly better, but the cyanosis, although less, persisted and he was admitted to the hospital on 12th September.

Condition on admission.—The patient on admission was markedly cyanosed; the skin and mucous membrane all had a definite bluish tinge. Besides a slight enlargement of the spleen nothing else abnormal was discovered. The heart and lungs were normal. The urine had a specific gravity of 1009 and contained no albumin nor sugar, but gave a strong reaction to indican. Urobilinogen was found in traces, but urobilin could not be detected even on spectroscopic examination.

A fresh blood film showed well-marked crenation of the red blood corpuscles, their colour being dichroic (yellow and green). No parasites could be found in the blood. On spectroscopic examination of the blood, bands of hæmoglobin could be seen, but neither methæmoglobin nor urobilin could be detected. The fragility of the blood was tested, with the following results:—

Initial hæmolysis .. 0.38 per cent. NaCl solution
Complete .. 0.28

This shows that the resistance of the red blood cells was slightly higher than normal.

The patient was put to bed, and given alkalies and mild purgatives daily.

Remarks.—The interesting points about this case are:—(1) The persistence of cyanosis which lasted for over nine days. Usually it disappears 24 hours after the drug is stopped, and very rarely lasts 7 days. (2) Although the blood was spectroscopically examined when the patient was distinctly blue, methæmoglobin, to the presence of which the cyanosis is attributed, could not be detected. (3) The resistance of red blood cells to hæmolytic agents was increased and not decreased, while the patient had plasmochin cyanosis.

TWO CASES OF PITYRIASIS RUBRA PILARIS

By M. N. PAI

CAPTAIN, I.M.S. (T.C.)

Indian Military Hospital, Poona

This disease is comparatively rare in India and the occurrence of two cases simultaneously is of more than passing interest.

Case I.—Sepoy, Umrao Sing, aged 20 years, was admitted into the Indian Military Hospital, Poona, on 22nd December, 1931, for a papular eruption on the body.

Previous history.—Nothing important and no members of his family have ever suffered from it. He used to perspire a good deal after exercise, but on 20th December, 1931, while in camp he caught a chill and next day noticed a papular eruption on the thighs and legs, which rapidly spread to the sides of his chest and abdomen, and the extensor surfaces of the upper extremities.

Condition on admission.—The patient is a well-built young man but with a general dryness of the skin of the body. The affected areas have a well-marked goose-flesh appearance and consist of follicular papules each about the size of a pinhead with a central horny plug surrounding a hair. These papules are well seen over the scapular regions, the extensor surfaces of the arms and forearms, the sides of the chest and over both the lower extremities. A few are also seen on the nape of the neck, but the scalp, face, front of the chest, fingers and the genitalia are completely free, and the palms and the soles do not show any hyperkeratosis. There is no itching or enlargement of glands and the Wassermann reaction is negative.

Microscopically each hair root was found surrounded by a horny plug of desiccated sebum.



Note the distribution of the papules.

Case II.—On 23rd December, 1931, Sepoy Gopal Singh noticed dryness of his thighs followed by the appearance of dry scaly horny papules. These extended gradually over both legs. Five days later he noticed follicular papules on the sides of the chest and abdomen, the extensor surfaces of both arms and forearms as well as over the shoulder blades. As in the previous case the scalp, face, front of chest, fingers, palms and soles are free. There is no itching and the Wassermann reaction is negative.

Differential diagnosis from:—

1. **Lichen Planus.**—This is preceded by itching, affects anterior aspect of trunk, forearms, wrists and genital organs. Papules are hard, shiny, yellowish-red in colour, flattened and depressed in the centre.

2. **Psoriasis.**—The scales are silvery and over-lapping.

3. **Dysidrosis.**—Occurs chiefly on hands and feet, sometimes on face and neck, but the typical aspect is seen on the fingers and itching is well marked.

Treatment.—Thyroid extract and arsenic internally, and alkaline baths externally have been tried with very little success.

Points of interest in these two cases are:—

1. The alleged sudden onset in both cases apparently due to exposure to cold while in camp.

17th July—Temperature—100°F. in the morning fell to normal by the evening. The jaundice became deeper, and he had bilious vomiting. Stools—brownish. Urine—8 ounces in 24 hours, hæmoglobin-coloured and highly acid, a trace of albumen.

Treatment.—Caffeine-soda-benzoas injection, hot water bag over loins, plasmoquine simplex—twice a day, alkaline mixture, etc.

18th July—Morning temperature—97.4°F. Pulse—96. Urine—1 ounce in 24 hours; last urine— $\frac{1}{2}$ ounce at 11 p.m. on the 17th. He had one liquid, bilious motion.

Rectal saline not retained. Pituitrin was injected.

9-30 A.M.—Catheter was passed after giving urotropin, grains 10. Not a drop of urine came out.

10 A.M.—A pint of intravenous alkaline saline was given by the direct method. The reaction was mild and lasted an hour. Adrenaline—minims 10, was given under tongue.

A liquid stool followed but no urine was passed.

11-30 A.M.—Temperature 97°F.

12 A.M.—He took a little milk and pine-apple.

During the temporary absence of the doctor who was watching the case, the patient walked out to the factory, a distance of about 500 yards. He was brought back to his house, where he swooned soon after and died at 1 p.m. from heart failure.

Case 2.—N. Ch. D., Hindu male, aged 20, garden assistant, Gopalpur Tea Estate, fell ill on 26th July, 1932.

Present history.—On 24th evening he went to a neighbouring garden and returned late at night. The next morning he had meat diet. At night he had a heavy meal and retired at 11 p.m. At about 2 A.M. he felt chilly and vomited undigested food. After a while he again got up from his bed and lay on the floor where he passed a stool. The doctor was called at 4 A.M. and he found the boy in a semi-conscious state.

Previous history.—He had been serving at Gopalpur for a year and a half. He had a few attacks of malaria, the last attack was in June 1932. He refused to take quinine regularly under the belief that quinine would produce blackwater fever.

26th July, 1932.—Morning temperature—101°F. Pulse—108. He was slightly jaundiced. Spleen—2 inches. Liver—not palpable. Tympanitis present. Patient drowsy. At 9 A.M. he passed about 4 ounces of hæmoglobin-coloured urine.

The treatment given was much the same as in the previous case. Only about 2 more ounces of urine were passed.

27th and 28th July.—Vigorous treatment was continued on the above lines but only $1\frac{1}{2}$ ounces of urine was withdrawn from the bladder by means of a catheter the first day and less than this on the second. The jaundice increased.

29th July.—The patient was intensely jaundiced—he passed no urine and only $2\frac{1}{2}$ drachms could be withdrawn by the catheter. He was fully conscious in the morning but despite every effort he died that evening at 8-37 p.m. His temperature chart is shown.

Case 3.—M. S., Hindu male, aged 28 years, garden assistant, Gopalpur Tea Estate.

Past history.—He was a malarial subject and had been serving in the Dooars for about 12 years.

Present illness.—He had been suffering from malaria for a fortnight. Since 23rd April, he had low fever in the evening and was taking alkali and quinine mixtures.

On 29th April, the temperature rose to 102.4°F. in the afternoon and in the evening came down to 99°F.

During the small hours of the morning of 30th April, 1930, the temperature rose to 103.6°F. and he passed hæmoglobin-coloured urine.

Spleen—up to umbilicus. Liver three fingers breadth below costal margin. Constipated. Slight jaundice present. Nausea and bilious vomiting.

He was treated on the same lines as the above cases. Intravenous saline produced a violent reaction but in an hour's time 10 ounces of clear alkaline urine was

passed. His temperature rose to 104.8°F. at 6 p.m. when 12 ounces of clear urine was again passed.

1st May, 1930.—Patient passed a restless night. Pulse was irregular. Morning temperature—97°F. Nausea—present. Two ounces of dark-coloured urine was passed at 3-20 A.M.; total in 24 hours had been 4 pints $5\frac{1}{2}$ ounces. After this he passed no urine. His temperature fell below 96°F. at 11-30 A.M. and he became unconscious and died at 12 noon.

A CASE OF ELEPHANTOID PENIS*

By M. G. RAMACHANDRA RAO, M.B. & C.M.

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THE patient, a student, aged 22 years, complained of thickening of the skin of the penis and scrotum, and enlargement of both.

Previous history.—Four years ago he used to get fever every month, his temperature shooting up to 103° or 104°F., and lasting about 12 hours. The fever started with a rigor, and pain all over the body. He had a burning sensation in his scrotum and penis. He had a course of sodium cacodylate injections and was relieved of the attacks for one year.

History of present illness.—The present condition started two years ago as a lymphangitis of the scrotum and penis, temperature running up to 104°F. and lasting



I. Before operation.

for about eight hours. Such attacks came on every month. At every attack he had swelling and tenderness in the scrotum and penis; the swelling increasing with each attack. He had an attack in October, but was free for six months from January to June 1931. He had a course of fibrolysin injections.

Condition on admission.—There is elephantoid thickening of the scrotum and penis. The skin is $\frac{1}{2}$ to $\frac{3}{4}$ inch in thickness; the skin of the penis is involved up to its root, and cannot be retracted. The meatus is not seen. The penis is shaped like a ram's horn, and the distal third is curved with the concavity of the curve pointing upwards, as seen in the illustration.

The length of the penis is about 8 inches from the tip to the root. The ram-horn curving of the penis has only occurred during the last year, and was not present from the start. The glans penis can be felt in the distal third of the elephantoid penis. When he passes urine

* Rearranged by the Editor.

2. Absence of tuberculous diathesis.
3. Absence of the characteristic papules on the scalp, face and front of chest.
4. Absence of hyperkeratosis of the palms and soles.
5. Absence of changes in the nails.

My grateful thanks are due to Col. E. C. Hodgson, D.S.O., K.H.P., I.M.S., Officer Commanding the Indian Military Hospital, Poona, not only for his kind advice but also for permission to publish the notes on these two cases.

THREE FATAL CASES OF BLACKWATER FEVER*

By C. C. DAS GUPTA, M.B.

Chief Medical Officer, Gopalpur Group of Tea Estates
Gopalbagan, Jalpaiguri

DURING the last ten years in the Dooars, I have treated a number of cases of blackwater fever, but the cases I am reporting here are in

to be blocked so completely that after saline not a drop of urine is secreted.

Case 1.—Boka, Chinaman, male, aged 50, carpenter, Gopalpur Tea Estate, got blackwater fever on 16th July, 1932.

Present illness.—At 11 A.M. he passed three ounces of hæmoglobin-coloured urine. His temperature was 105°F., pulse 116, and respiration 36. He had intense jaundice. His bowels were constipated, and tongue coated. The liver and spleen were not enlarged.

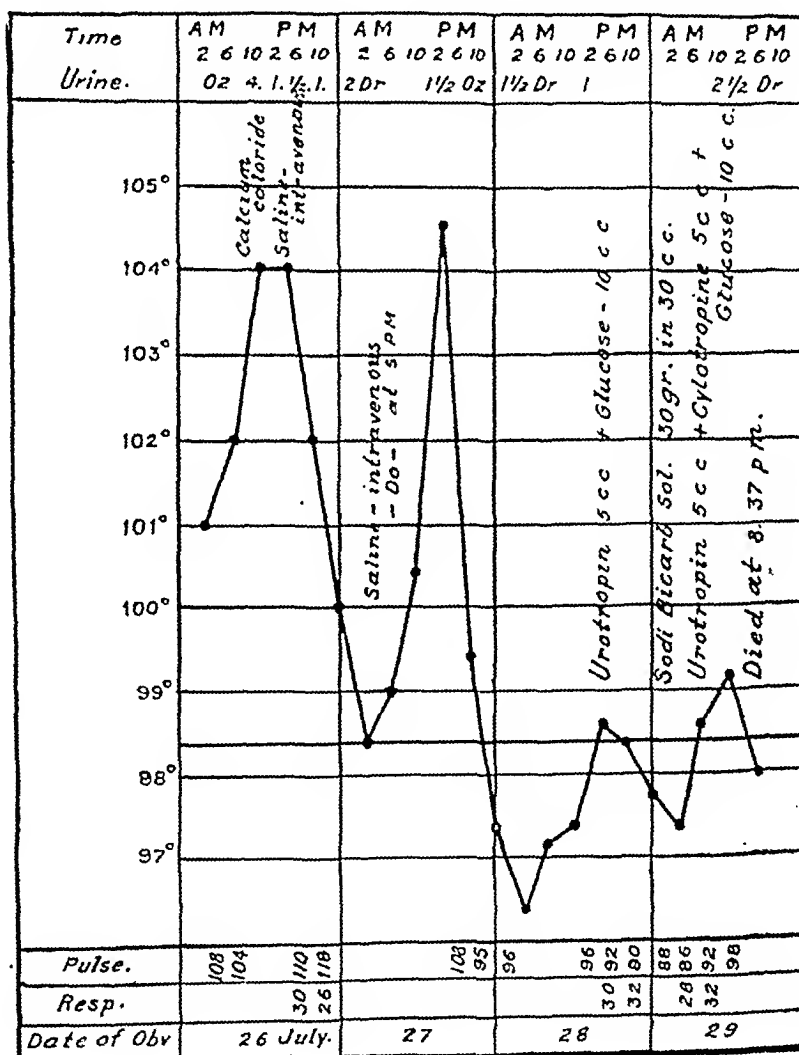
Past history.—He had lived in the Dooars for 18 years and had had 8 attacks of blackwater fever, the last attack was on 3rd October, 1931. He was a malarial subject and did not take quinine as a prophylactic.

On 7th July, 1932, he had an attack of malaria and was put on saline purge, alkali and quinine. He got well in a few days and resumed his duties.

16th July, 1932—Treatment—(1) An initial purgative containing calomel—grs. 2 and sodium bicarbonate—grs. 10, followed by magnesium sulphate at bed time, was given.

(2) An alkaline mixture—a combination of sodium bicarbonate, potassium citrate, liquor hydrargyri perchloridi and extractum punarnavæ liquidum—every 2 hours.

Name... N.C. Das. Age... 20. Disease... Blackwater Fever.



a class by themselves and in spite of every possible treatment ended fatally.

This season cases are occurring which start with anuria and die of uræmia, in spite of intravenous alkaline saline. The kidneys appear

(3) Rectal saline—sodium chloride—90 grains and sodium bicarbonate—160 grains to the ounce of water—6 ounces every 2 hours.

(4) Calcium chloride—grs. 4 in 10 cubic centimetres glucose solution was given intravenously.

(5) Plasmoquine simplex—1/6th grain—one dose.
Diet—green-cocoanut water, soda water, glucose and sodium bicarbonate drink.

* Rearranged by the Editor.

Indian Medical Gazette

JANUARY

RECENT RESEARCHES ON BLACKWATER FEVER

A VERY important memoir which has recently appeared on the subject of blackwater fever is that by G. R. Ross (1932), Rhodesian Research Fellow of the London School of Hygiene and Tropical Medicine, entitled 'Researches on Blackwater Fever in Southern Rhodesia'. This memoir is very comprehensive, both in its survey of the previous literature and in its account of the investigations in Rhodesia carried out by the author and his collaborators. It constitutes an extension of the now classical memoir by Thomson in 1924.

The white occupation of Southern Rhodesia dates from 1890 and the successful development of the country has been dependent on the two primary producing industries of mining and agriculture. The white population numbers 44,950, of which some 8 per cent. are engaged in mining industries, 17 per cent. in agriculture, and 75 per cent. in transport, industrial, commercial and professional duties. This last element is largely concentrated in the four large towns of Salisbury, Bulawayo, Gwelo and Umtali in which approximately 47 per cent. of the white population live. Males largely outnumber females, and owing to the immigration of young adults the percentage of the white population over 15 years of age is greater than it is in the standard British million. The native population numbers 933,899, of which 760,301 live in the native 'reserves' and 173,598 live and work in close proximity to the white population.

As the result of Thomson's work on the subject in Southern Rhodesia in 1922 and 1923 a standard system of notification of blackwater fever cases was introduced (although not made compulsory), and this greatly helped Dr. Ross in collecting data. Between the years 1914 and 1928 inclusive 679 cases of blackwater fever were treated in Southern Rhodesian hospitals with 152 deaths, a case mortality of 22.2 per cent. The average death rate among the European community between 1924 and 1928 was 9.25 per mille, of which blackwater fever, notified as such, accounted for 2.2 per cent. of the total deaths. The disease is nearly four times as common among European males as among European females, but the population of the latter only numbered 17,366 in 1926

which would account for the discrepancy. Essentially, blackwater fever attacks those engaged in the rural areas—the case incidence per mille being 3.01 for those engaged in agriculture, 2.83 for the mining industry, and 2.07 for transport workers; 1.42 for rural areas, 1.32 for rural townships, and 0.28 for urban areas of over 1,000 population.

In summing up the first section of the memoir, on the distribution and incidence of the disease in Southern Rhodesia, Dr. Ross writes as follows:

'The essential fact which has emerged in the study is, probably, the realization of the intimate association of the disease with rural conditions. The higher incidence of the disease in rural inhabitants as compared with urban inhabitants generally, and the high incidence in those engaged in pioneer occupations, both help to establish this fact.

The differential distribution in urban and rural districts deserves to receive emphatic mention, since it is an encouragement to the hope that the disease may yet be more fully controlled. This history of the four big urban centres shows that in the earlier years of the colony, blackwater fever was not always the comparatively rare disease that it is to-day. Perhaps the most illuminating part of the story of their achievement of relative immunity is the realization that this has come about, not because of special control measures against the disease, but as part and parcel of their general economic and municipal development. That this should be so, is surely sufficient encouragement for the belief that as development in the country districts proceeds we may look for a lowered incidence of the disease in the next, if not in the present generation. Further, the application of methods of control, based on conclusions reached by the scientific study of the disease, must assuredly promise a speedier path to the desired consummation.

This definite distinction between urban and rural areas must enter largely into the consideration of several features of the distribution of the disease as revealed in the preceding pages. Thus the fact that the incidence is greater in males than in females may be explained, partially at least, by the fact that men are much more likely to engage in the occupations which bring them into contact with primitive and undeveloped country. Farming, mining, prospecting and transport work which supply so large a percentage of the cases of the disease, are still almost entirely the undisputed territory of man in Southern Rhodesia. At the same time it must be acknowledged that wives and other female relatives do in many instances share the hardships and primitive environment under which these industries are conducted. There is no method of obtaining the relative figures of females so placed or calculating the incidence of the disease in them, but the cases of the disease recorded in females for the period have occurred almost exclusively in this class.

Another factor which may account for the difference in incidence in the two sexes is the fact that men are much more careless in their habits and methods of life than women. The flimsy and primitive housing arrangements, the monotonous and inadequate dietary that consists mainly of tinned products and ignores such essentials as fresh milk or vegetables, and the general disregard of comfort-making amenities, that so often characterize life under masculine management, are not tolerated by women, if anything better is possible, and their influence in raising the general standard of life cannot be minimized. That they generally insist on a high standard may be one reason why the incidence of the disease amongst them is less.

As far as the age-distribution of the disease is concerned, attacks may occur at any age, but the figures for the period have shown the disease to be rare in

* Ross, G. R. (1932). Researches on Blackwater Fever in Southern Rhodesia. No. 6 of the *Memoir Series of the London School of Hygiene and Tropical Medicine*. Price: cloth 10s. 6d.; paper 8s.

those under 5 years of age and to be commonest in the years of adult life, particularly from 15 to 34. The explanation of the low incidence in the years of childhood probably lies in the fact that much greater care and attention are very naturally lavished on children who are thus protected from unhealthy circumstances as far as possible, and that the majority spend a large proportion of their childhood in the schools which are mostly situated in the non-endemic urban areas. The increased incidence in adult years is probably accounted for by the fact that it is during these years that occupations are engaged in which spell risk as far as blackwater fever is concerned.

The incidence of the disease in the Rhodesian-born is illuminating in this connection, for it is seen that the chances of contracting the disease are small until an age is reached when economic circumstances force them to seek employment, and to look after themselves.

The relationship of length of residence to the development of the disease involves considerations which are different from those discussed above, for the establishment of the fact that the disease only occurs after a certain length of residence is bound up with the question of the aetiology of the disease in a more intimate way than the distribution of the disease amongst the various sections of the community. The figures obtainable for the five years have shown that the greatest percentage of first attacks occurs during the first five years of residence, that the disease has been uncommon in those with less than one year's residence. These findings are in agreement with experience elsewhere, but it is hardly possible to discuss any explanation of why this should be so without reference to other considerations which have not yet been discussed.

The author passes next to a consideration of the relationship of blackwater fever to meteorological conditions in Southern Rhodesia. In general, the incidence of the disease reaches its maximum about three months after the period of maximum rainfall (October to March). Correlation with temperature is less marked, though the incidence tends to be highest in those regions with highest temperature. 'Viewing the subject as a whole, the impression that is gained is that the influence that meteorological conditions exert upon the disease is not a direct one, but is dependent upon the activity of some other factor upon which they react'.

Chapter IV of the memoir deals with the relationship of blackwater fever to malaria, and here we reach the crux of the whole question. The accumulated evidence in this chapter is conclusive that blackwater fever is a manifestation of malaria. Deeks and James (1911) in Panama were perhaps the first to stress this point. Schilling (1911) in German East Africa also drew attention to it. In some areas, such as the Punjab and the Philippine Islands, we get intense malaria without blackwater fever, but in the former, malaria is strictly seasonal in its incidence and the population is not exposed to infection throughout the year, whilst in the latter, malaria control and continued treatment are fairly well enforced. In Rhodesia malaria is not a notifiable disease, and very many cases do not come to hospital. On the other hand chart 14 of the memoir shows how extremely close is the correlation between hospital admissions for the years 1924-1928 from malaria and those from blackwater fever,

whereas the curves for admissions for typhoid fever and pneumonia show no such correlationship at all. (This graph confirms and extends an exactly similar set of observations recorded in Thomson's memoir of 1924.) Chart 12 in the memoir shows again an extremely close correlationship between the prevalence of the local anophelines, which reaches its maximum in March, and blackwater fever, which reaches its maximum in April. The malaria of Southern Rhodesia is almost exclusively due to *Plasmodium falciparum*, whilst of the 14 species of Anopheles present, the two really important ones are *A. funestus* and *A. gambiae*, whose prevalence again shows a very close relationship to that of blackwater fever, and which alone on mosquito dissections proved to be malaria-infected. The work of Napier and Campbell (1932) and of Knowles and Das Gupta (1932) shows that hæmoglobinuric fever may occur as a terminal event in monkeys of species *Macaca mulatta* dying from monkey-malaria, and again emphasises the close relationship between plasmodium infections and blackwater fever.

It must be admitted on the whole that the 'malaria hypothesis' with regard to the etiology of blackwater fever now holds the field to the exclusion of any other. (The reviewer has tried to hold an open mind on this subject for years, but is now forced to the conclusion that this hypothesis is the correct one.) The association is usually with *P. falciparum* infections, and that in an endemic or hyperendemic area, but sometimes the other species are concerned. Thus, Giglioli (1930) stresses its connection in British Guiana with *P. vivax* infections, whilst workers in the Dutch East Indies have found it associated with *P. malariae* infections.

If blackwater fever is a manifestation of malaria, it is due however to malaria plus some other factor or factors. What this factor or these factors are at present we do not know. There may be exaltation of the virus by constant passage through aboriginal tribes in the locality who have become habituated to it; it may be associated with certain groups of transmitting anophelines; it may be precipitated by quinine (but not necessarily so in all cases); it may be due to biological or biochemical causes in the individuals concerned. The future study of the disease in experimental monkeys may help us in investigating these factors.

With regard to the association of blackwater fever in Southern Rhodesia with malaria, Dr. Ross writes as follows:—

'As far as Southern Rhodesia is concerned the relationship existing between malaria and blackwater fever in that territory must be regarded as adding considerable weight to the argument that the latter disease is a manifestation of infection with malignant tertian malaria. It has been seen that the greatest incidence of blackwater fever occurs in those classes of the population and in those areas in which the incidence of malaria is greatest, that freedom from malaria and blackwater fever go hand-in-hand, that the seasonal

incidence of the two diseases is similar, that evidence of previous malarial infection exists in practically every case of blackwater fever, and that there is an intimate association between an attack of acute malaria and an attack of hæmoglobinuria. The collective weight of these facts must surely emphasize the importance of malaria in the genesis of the disease. How far infection with other varieties of the malarial parasite can predispose to the development of blackwater fever cannot be determined from the information obtainable from Rhodesia, where malignant tertian malaria alone accounts for practically all cases of malaria seen.

If one takes certain features of the epidemiology of the two diseases, particularly the distribution in the population and the seasonal incidence, the similarity which has been demonstrated might be explained by a common vector. Thus the transmission by *Anopheles gambiae* or *Anopheles funestus* of a hypothetical blackwater-fever virus, in addition to the malarial parasite, would explain the absence of both diseases from districts in which these mosquitoes were absent and the occurrence of the epidemic phases of both diseases at the same time of year. Such an assumption, however, cannot explain the infrequency of blackwater fever in the first year of residence or its development at considerable intervals after removal from an endemic region unless one postulates qualities in the virus or agent of a most unique nature. Nor can it explain the immunity of the native inhabitant or the frequency with which an attack of malaria precedes the attack of blackwater fever.

The conclusion reached by Leishman (1912), Deeks and James (1911), Stephens (1915), Thomson (1924), and many other observers that blackwater fever is a manifestation of malarial toxicity is one which the results of the present investigation substantiate.

With regard to the rôle of quinine, Dr. Ross reports in all on 162 cases, which gave the following history:

No quinine taken for at least one week prior to the onset of blackwater	11 cases.
Patients regularly taking prophylactic quinine	20 "
One dose only of quinine taken prior to the onset of blackwater	31 "
Hæmoglobinuria developed after several doses of quinine had been taken	100 "

'The obvious irregularity in the relationship of quinine to the attack', he writes, 'in so great a number of cases presents a perplexing problem if we are to regard quinine as an important factor in the actual genesis of blackwater fever and suggests that the mechanism whereby the effect is produced is of a complex nature'.

The author deals next with other subsidiary factors. The Rhodesian cases do not bring out exposure to cold or fatigue as exciting causes. In some instances a well-marked familial history was obtained (but this may be due to members of the same family residing in the same house). A history of previous attacks is common—73 out of 192 cases reported, or 38 per cent. It is well known that blackwater fever is frequently a household or site infection, the type of house concerned being usually one that affords ideal facilities for resting mosquitoes.

Part II of the report deals with the biochemistry of the blood and urine in blackwater fever. Here, again, there is an admirable summary of all previous work and views, and a large volume of original work reported on. It is impossible to summarise this section of the report, since it is itself of the nature of a review, and should be read in the original by all workers interested in the disease. Part III of the memoir is concerned with clinical types of the disease, its prophylaxis and treatment. Such types are exemplified as mild to moderate and uncomplicated, fulminant and toxic types, the anuric type, the continued and intermittent type. Of 118 cases the duration of the hæmoglobinuria was as follows:

Up to 24 hours	29
1—2 days	28
2—3 days	27
3—4 days	16
4 days or longer	18

Relapses were not infrequent—10 per cent., as compared with a figure of 13 per cent. for a series of cases in Uganda. The opinion is often expressed that blackwater fever patients should not be moved to hospital as this increases the risk run. Dr. Ross finds that the reverse is the case; the case mortality among those moved to hospital was 27 per cent. as against 32 per cent. for those not moved; the greater nursing facilities in a good hospital more than compensate for the risk incurred in moving the patient.

With regard to symptoms, rigor may be absent—48 cases, may precede the hæmoglobinuria—104 cases, or follow it—10 cases. The administration of quinine has no effect on the pyrexia accompanying the hæmoglobinuria or upon 'post-hæmoglobinuric pyrexia'—the pyrexia itself being apparently a manifestation of the hæmolytic process. Hiccough is common in the anuric and toxic cases and is a very grave symptom. Lumbar pain is very frequent and would seem to be definitely of renal origin. Pain over the hepatic area and spleen may also be complained of. Splenic enlargement is usual but not invariable in the disease.

With regard to treatment, there are so many 'treatments' in vogue that it may be said at once that none of them has any special merit. The mortality in the disease remains at a figure of about 25 per cent., no matter what treatment is adopted. Injections of hæmostatic sera, of horse serum, of antivenene, and blood transfusion have all been advocated, but the benefit of all seems doubtful. Calcium chloride may be anti-hæmolytic in the test tube, but it is more than doubtful whether the amount injected could achieve the same effect in the human body. Intramuscular injections of caffeine sodium benzoate were tried out in a series of the Rhodesian cases, but of 20 cases so treated 8 died. 'The conclusion reached by most

observers who have had to undertake the treatment of blackwater fever is, undoubtedly, that we possess no remedy which can be accepted as having demonstrable influence on hæmolysis, and this conclusion is reflected in the fact that the treatment most generally employed in the disease is purely symptomatic'.

'To endeavour to produce diuresis is undoubtedly physiologically sound', writes the author. Sodium bicarbonate has been used extensively in the treatment of the disease for a variety of reasons. 'The alkaline treatment of blackwater fever has received most extensive publicity and there is some danger of its being regarded as a panacea. One fact, however, deserves emphasis. Despite the number of authors who have published their findings the total number of cases covered by their reports is small..... There is thus ample justification for the critical to wonder whether the ordinary probability of recovery is sufficiently allowed for..... If alkaline therapy is used, the oral or rectal route is to be preferred to the intravenous. Intravenous injections of large quantities of sodium bicarbonate are undoubtedly dangerous and may cause tetany and even death..... In Southern Rhodesia the intravenous injection of bicarbonate in cases in which symptoms of suppression were present was attended by disappointing results. Used in the strength of 150 grains to the pint, the injection of 1 and 2 pint amounts was ineffectual in preventing the development of suppression in three cases of the anuric type'. Further, in blackwater fever, although there has been a loss in the corpuscular volume of the blood there has been no corresponding loss in the plasma, and there do not appear to be special indications for intravenous saline injections. Blood transfusion would appear to be much better. Treatment after the cessation of hæmoglobinuria resolves itself into treatment of the anæmia and of the resulting debility. Iron and arsenic are universally employed in this condition, whilst treatment of the anæmia with liver extract is also worthy of trial.

With regard to the very vexed question of whether the administration of quinine is advisable or justifiable during blackwater fever or not, it seems impossible to give a definite opinion. The largest collection of figures on this point is that given by Thomson (1924) compiled from the statistics of Deaderick and Cardamatis: in 1,931 cases treated with quinine the mortality was 25 per cent., whereas in 898 cases treated without quinine the mortality was 10.3 per cent. (It seems possible that in atabrin we may now possess a drug which will clear up the malaria infection underlying the blackwater fever without any danger of increasing the hæmolysis.) After recovery from the attack of blackwater fever, anti-malaria treatment must be given, or the patient will get a relapse—either of malaria or of blackwater fever,

With regard to prophylaxis, the position is the same as that with regard to malaria. In the tremendously widely scattered rural areas of Southern Rhodesia larval species control is an immensely difficult problem; and individual prophylactic measures (amongst which the administration of plasmoquine for its 'crescenticidal' effect will certainly take its place) seem to be more feasible. The screening of houses is not merely advisable, but is a necessity. In this connection Dr. Ross writes as follows:

'It is obvious that no campaign against malaria can be planned without knowledge of topographical circumstances, of the distribution and nature of the exposed population, the habits of the carrier mosquitoes, and the economic problems involved. In Southern Rhodesia we have to deal with an extensive territory in which the exposed population is small, widely scattered, and consists mainly of two races differing greatly in their habits and circumstances. Moreover, it has been shown that the disease is essentially rural in its distribution and that it exhibits a seasonal periodicity which is closely related to the prevalence of *Anopheles gambiae* and *Anopheles funestus*. It has further to be remembered that the country is still in the initial stages of its growth and development, and that, however great the desire to be rid of malaria, there is a limit to the expenditure which can be devoted to the object. Taking these facts into consideration, it does not seem probable that extensive anti-larval measures will be instituted in the near future. If the problem were the elimination of malaria from such towns as Salisbury and Bulawayo one would not hesitate to recommend such schemes for favourable consideration, but when the main endeavour must be to protect the scattered rural population economic problems are likely to cause the postponement of a national effort to a more prosperous time. This applies most particularly to drainage schemes, the value of which is not challenged, and where individuals or companies are in a position to embark on such schemes the expenditure would undoubtedly be justified.

Alternative methods of larval control involving the employment of such larvicides as oil or Paris green seem more suitable to the requirements of the country. The investigations on mosquito prevalence in Rhodesia suggest that such measures are only essential during the rainy season and for a short period at the commencement of the dry season, and they may be recommended as more likely to achieve a quicker and more extensive result under present conditions than any other anti-larval measure.

While the merit of anti-larval measures remains unquestioned, it would appear that considerable time must elapse before such measures will effect any considerable reduction in the mosquito population of the colony, and that, meantime, the inhabitants in rural districts must depend upon more personal methods of prophylaxis.

While on the whole, the standard of education in the colony is such that the elementary facts of the mosquito-malaria doctrine do not require stressing, there is urgent need for the instillation of a more wholesome respect for the consequence of malarial infection. The general attitude towards the disease is much too complacent. It is regarded as a demon not half so black as terroristic medical men would paint it, and its exorcism by an occasional dose of quinine as a matter of simple household therapeutics. Until such time as the individual is brought to realize that malaria is an insidious, treacherous and death-dealing disease, only a half-hearted response may be expected from those whose co-operation is an essential in any campaign against it,

Much greater attention should be given to the choice of building sites and the construction of mosquito-proof houses. The choice of sites situated as far as possible from possible anopheles breeding grounds, the clearing of scrub vegetation, and the removal of native compounds to a distance of at least 400 yards on the leeward side are elementary precautions which all should observe. As far as actual construction is concerned, the necessity of screening part of the house at least should be recognized, while mosquito-nets should be regarded as an essential furnishing.

The London School of Hygiene and Tropical Medicine is to be congratulated on the publication of this admirable report. Within its 262 pages it summarises our present-day knowledge of blackwater fever, with special reference to rural areas, and emphasises the lacunæ in that knowledge. It should serve as a starting point from which further investigation will commence.

R. K.

REFERENCES

Deeks, W. E., and James, W. M. (1911). *A Report on Hæmoglobinuric Fever in the Canal Zone*. Mount Hope, C. Z., p. 177.

Giglioli, G. (1930). *Malarial Nephritis*. Messrs. J. & A. Churchill, London.

Knowles, R., and Das Gupta, B. M. (1932). A Study of Monkey-Malaria, and Its Experimental Transmission to Man. *Indian Med. Gaz.*, LXVII, p. 301.

Napier, L. E., and Campbell, H. G. M. (1932). Observations on a Plasmodium Infection which causes Hæmoglobinuria in Certain Species of Monkey. *Indian Med. Gaz.*, LXVII, p. 246.

Schilling, C. (1911). In Ross' *Prevention of Malaria*. London. Pp. 451-474.

Thomson, J. G. (1924). Researches on Blackwater Fever in Southern Rhodesia. *London School of Tropical Medicine: Research Memoir Series*, Vol. VI, London, p. 149.

Special Articles

SPLENECTOMY. INDICATIONS AND RESULTS, WITH SPECIAL REFERENCE TO CONDITIONS OBTAINING IN THE TROPICS*

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It is proposed to bring before you, very briefly, some facts with regard to the subject of splenectomy, with special reference to tropical countries. This must include some account of the enormous and complicated subject of splenomegaly. The short notice I have received to join in this discussion is quite inadequate for a full account of this subject.

In order to interpret correctly the indications for splenectomy, we must have sufficient knowledge to unravel the clinical and pathological evidence which comes before us. This knowledge is to a great extent in the making, more especially in the tropics. Taking India as an example of the tropical and sub-tropical world, we find an enormous amount of material for investigation. What is wanting, however, is the necessary co-operation between the physician, surgeon, and pathologist. My own small efforts to elucidate the subject from a surgical point of view and my long connection with medical colleges in India have shown me that India is very backward in this respect. Most valuable clinical and research work has been done, but with little effort towards collaboration.

In Egypt surgeons number their splenectomies by the hundred, but they have the advantage

of dealing with a definite clinical entity, Egyptian splenomegaly. But even in this disease the pathology has not been accurately worked out, although its association with *Bilharzia mansoni* seems to be established. The splenomegaly of chronic malaria and kala-azar, when it approaches the so-called splenic anæmia stage, would appear to be of a closely allied type.

From the point of view of the patient we can unhesitatingly state that he is entitled to surgical treatment for splenomegaly as soon as it is apparent that therapeutic measures are of no avail, provided that the surgeon after weighing the indications for operative treatment can offer him a reasonable chance of improvement or cure. Although our knowledge is making rapid strides, it is true to-day that the surgeon is not in a position to be able to say in every case whether splenectomy offers the patient the best hopes of recovery. Two essential factors have still to be worked out, namely, earlier and more accurate diagnosis and a more successful procedure for dealing with fibrosed spleens with extensive adhesions.

It is not intended to deal at any length with the indications and results of splenectomy for such conditions as injuries, displacements, abscesses, tumours and cysts. These present few features of peculiar interest in tropical countries. India is the land of *ruptured spleens*, because of the enormous incidence of malarial enlargement. Chevers (1870) noted as far back as 1866 that among 33 police autopsies in that year in one small district (Jessore), six were cases of ruptured spleens. The accident is more common during the months of highest malarial incidence, August to November. It is well known that malarial and kala-azar spleens may be ruptured by comparatively trivial

* Read in the Section of Surgery at the Centenary Meeting of the British Medical Association, London, 1932.

violence, and that so-called spontaneous rupture may be caused by such slight muscular effort as turning over in bed.

In a series of 45 consecutive cases of ruptured spleens treated by splenectomy collected from the records of three hospitals in India and Burma the difficulties of exact diagnosis are evident. Pain, tenderness, and localized dullness in the left flank are the most reliable signs. The character of the pulse and the presence or absence of rigidity or distension are not of great diagnostic value. It is obvious that the symptoms and signs in each case will depend much upon the size and consistency of the spleen, its degree of fixity, and the nature of the violence. In 22 cases of this series in which the nature of the violence is recorded, the rupture was due to crushing in 7, falls in 6, blows in 7, stabs in 2, and in one case of sarcoma the rupture was said to be 'spontaneous'. It must be borne in mind that in the tropics a large proportion of ruptures occur in spleens already enlarged by disease. The results of splenectomy in these 45 cases was: recovered 26, died 19. The best results were obtained among those operated on promptly, that is to say as soon as the effects of the primary shock had abated. Transfusion would undoubtedly have saved some lives, but this procedure is not always possible in India. Several cases in

was much elongated and twisted two and a half times, so that the notched border lay posteriorly beyond the reach of palpation. The viscus was greatly distended with blood and the splenic vessels were very large; in one case strangulation had threatened on two occasions.

Abscesses, cysts, and new growths of the spleens are all rare conditions. The pus in abscesses is usually grumous or thick and creamy, and is most often sterile on culture. Hæmorrhagic cysts may result from the breaking down of soft malarial spleens and later on these may degenerate into abscesses. Hydatid cysts are very uncommon as are all varieties of new growth; in one case of sarcoma of the spleen, referred to again below, the organ weighed 15 lbs. 14½ oz., and invaded the ribs and surrounding structures with secondary growths in the kidneys.

Three groups of post-mortem cases will now be discussed with the object of trying to elicit information as to the ætiology of splenomegaly in the East. They comprise over twelve hundred cases of enlargement of the spleen occurring among 3,308 consecutive deaths from all causes. Many cases of splenomegaly in which death occurred from rupture or other causes soon after admission into hospital have escaped notice here, as the necropsy was performed in the police morgue.

TABLE I

	Series A (Bengal) 1920—1929: 977 cases. Minimum wt., 200 gm. Highest wt., 2,700 gm. Spleen enlarged, 54 per cent. Based on ante-mortem diagnosis	Series B (Bombay) 1927—1931: 700 cases. Minimum wt., 150 gm. Highest wt., 2,030 gm. Spleen enlarged, 40 per cent. Based on autopsy findings	Series C (Rangoon) 1927—1931: 1,631 cases. Minimum wt., 200 gm. Highest wt., 8,144 gm. Spleen enlarged, 29 per cent. Based on autopsy findings
Malaria	31	49 (including 7 ruptured)	30
Kala-azar	67	1	1
Portal cirrhosis	19	..	40 (17 with ascites)
Acute infections, etc.	104	42	241
Tuberculosis	88	..	85 (11 involving spleen)
Leukæmia	3	1	1
Hodgkin's disease	1	2	..
Pernicious anæmia	4	..
Heart disease	38	9	31
Splenomegaly of doubtful ætiology	26	2	1
Sarcoma of spleen	2
Miscellaneous	148	170	38
TOTAL ..	525	280	470

which the extravasated blood was re-injected into the patient during the laparotomy appeared to be greatly benefited.

Very movable or wandering spleens are more often met with in tropical than in temperate countries, as would be expected. The difficulties of diagnosis in some instances are considerable. Two very large spleens of this type were operated on by me as undiagnosed tumours and both did well. The pedicle in each case

These three groups of splenomegaly are compared with difficulty, because they are not all classified on the same basis. A brief analysis will however be attempted.

Series 'A' includes 525 cases of enlarged spleen found in 977 autopsies (54 per cent.), taking 200 grammes as the minimum for enlargement, from the Pathological Department, Calcutta Medical College, collected by M. N. De (1932). The classification given above in

table I is based on the ante-mortem diagnosis, but the following is a brief summary of some of the autopsy findings as analysed by De :

(1) There are 54 examples of splenomegaly in the whole series in which the weight of the spleen varies between 600 grm. and 2,700 grm., and in these the post-mortem findings are as follows :—

Kala-azar cirrhosis	14
Splenic anæmia	2
Kala-azar or chronic malaria suspected, but not confirmed	21
No definite diagnosis	17

De states that these 17 cases of unknown ætiology and the 21 diagnosed as malaria or kala-azar without post-mortem confirmation, form a natural group presenting a recognizable clinical history :

‘They are commonest in the western and the lower part of East Bengal and run a chronic course, with gradual enlargement of the spleen and liver accompanied by irregular fever. Ordinary therapeutic measures are of no avail. They develop a secondary anæmia with leucopenia and a reduced polymorph count; fibrosis of the liver develops leading up to ascites. Death supervenes from some inter-current malady, such as pneumonia, colitis, etc.’

The morbid anatomy and histopathology of the same group of cases with very large spleens is described by De as follows :—

‘The spleen is tough on section with prominent trabeculae, and perisplenitis and adhesions are common; the liver is congested, fibrosed, or cirrhotic (lobnailed); red formative marrow is found in the middle third of the femur. Histologically: the spleen pattern is lost and the Malpighian follicles atrophied; the pulp cellular and filled with many large phagocytic cells; red cell phagocytosis may be prominent. The capsule and trabeculae are found thickened with increase of coarse reticular fibres’.

If the existence of this natural group of very large spleens, with characteristics as described by De above, can be confirmed and it can be proved that such cases are recognizable by clinical or other tests, then the possibility for a large field for splenectomy comes into view. What would be the results of surgical interference remains to be seen, but this will probably depend mainly on two factors: the possibility of raising the patient's powers of resistance before operation, and the improvement of the existing technique for dealing with extensive splenic adhesions.

If we proceed to criticize the pathological findings of De in these 54 cases of greatly enlarged spleens, the striking fact is observed that none of them are accepted as cases of chronic malaria. Malaria is known to be common in Bengal and to be associated with considerable splenomegaly, and it seems fair to conclude that a certain number of cases are included in this group of undiagnosed cases.

T. A. Hughes and D. L. Shrivastava (1931) have published a report of 31 cases of anæmia in patients with splenomegaly, which is ascribed to chronic malaria although no signs of active malaria or parasites were present. In the absence of parasites and of active malaria and in some other respects these cases resemble De's group of undiagnosed splenomegalies. Hughes and Shrivastava describe their series of cases further as follows: they were all admitted into hospital with a clinical history of repeated attacks of fever followed by progressive weakness, intensified by the discomfort of carrying very large spleens; in some cases the liver was also enlarged, and in two which reached the post-mortem room the spleens presented the typical appearance of chronic malaria. A detailed report is given of the blood examination of these patients by Hughes and Shrivastava, and it is concluded that in the milder cases the blood condition is due to the destruction of the erythrocytes by the reticulo-endothelial cells of the spleen and possibly of other organs, facilitated in some cases by the abnormal fragility of the corpuscles. In severe cases there is evidence of derangement of the bone marrow. While malaria is given as the primary cause of this type of anæmia associated with splenomegaly, it is suggested that there are also aggravating causes such as dietetic deficiencies, the strain of pregnancy, etc. Of four cases treated with liver and iron improvement took place in three, but in the fourth no improvement occurred in the red cells or hæmoglobin, although there was evidence of bone-marrow activity, suggesting that blood destruction kept pace with blood regeneration. This view was supported by the behaviour of the plasma bilirubin. Splenectomy was not performed for any of this series, but it would certainly appear a reasonable procedure in cases such as these where the spleen is dominating the pathological situation instead of subserving useful functions. A further argument in favour of splenectomy is that it is in accordance with experience that patients of this type improve while under therapeutic treatment, but retrogress as soon as this is discontinued.

The characters of the splenomegaly of kala-azar must also be considered in connection with the ætiology of doubtful cases of splenic enlargement. It is generally stated that in kala-azar the spleen has a thickened capsule and the microscope shows an increase of fibrous tissue, but this is not borne out by critical examination of active cases. In a series of 31 cases of enlarged spleen occurring during a period of nine years, the connective tissue and reticulum of the liver and spleen were carefully studied by Shanks and De (1931). The greatly enlarged spleens were found to be chiefly due to kala-azar, and in 25 the parasite was identified. In 23 of the parasite-positive cases no increase of the fibrous tissue or reticulum was demonstrable, while in 5 parasite-negative cases

there was evidence of fibrosis. In 70 per cent. of the same positive series there was no increase of the fibrous tissue or reticulum of the liver. These soft positive kala-azar spleens are wonderfully responsive to therapeutic measures and the question of splenectomy does not arise, but it is known that in more chronic cases the spleen may become much more fibrous and diminish little in size under treatment (Napier). Christophers refers to patients with very large spleens without parasites, but resembling cases of kala-azar in every other respect; and others without any clinical resemblance to kala-azar, but with a splenomegaly exactly like that of kala-azar.

These post-malarial and post-kala-azar splenomegalies are well worthy of a close study among the group of cases of doubtful aetiology from the point of view of treatment by splenectomy. These are some of the cases which would appear to degenerate into the 'splenic anaemia' stage and become a menace to health.

Before leaving the Bengal group of 525 cases of splenomegaly it is interesting to note that there were 26 cases in which accessory spleens were present; and that in 203 instances fibrosis of the spleen was a prominent feature, with thickened capsule, peri-splenitis, adhesions, thickened trabeculae, dull to dark red colour. There was no evidence of any direct relationship between the degree of enlargement and the amount of fibrosis.

Series 'B' (Bombay) includes 280 cases of splenomegaly in 700 consecutive autopsies (40 per cent.), taking 150 gm. as the minimum weight, collected by P. V. Gharpure at the Pathological Department, Grant Medical College, Bombay. The classification adopted by Gharpure (see table I) is based on the post-mortem findings and is not intended to be a complete analysis of the cases. Its object is to compare and contrast the Bombay group with the Bengal group, especially as regards the incidence of malaria, kala-azar, portal cirrhosis, and splenomegaly of unknown origin.

The series presents some interesting features of its own. There are no cases of kala-azar, and it is known that this disease is absent in the western half of India. Chronic malaria with fibrosis of the spleen is responsible for 45 cases (16 per cent.) of enlargements, and it is stated that peri-splenitis and adhesions are usually present in this disease. Cirrhosis of the liver was not found associated with splenomegaly, and the high incidence of malaria suggests the conclusion that malaria is not a causal factor in the production of cirrhosis of the liver.

Series 'C' (Rangoon) comprises 470 cases of splenomegaly among 1,631 autopsies performed at the Rangoon General Hospital (29 per cent.). A rough classification has been attempted based on the cause of death found at the necropsy. Acute or chronic malaria accounts for 30 cases (6 per cent.), and this

series like the Bengal series shows a high incidence of cirrhosis of the liver with or without ascites, 40 cases (9 per cent.). Tuberculosis, probably in most cases an intercurrent affection, accounts for 85 cases (18 per cent.), and acute affections and miscellaneous conditions together total 59 per cent.; there were two cases of sarcoma of the spleen.

If we consider the largest spleens only in this series, 63 in number, weighing 600 gm. and upwards, we find the post-mortem diagnosis of cirrhosis of the liver in about 38 per cent. and malaria in another 14 per cent. Of the remainder about 40 per cent. appear to be caused by diseases such as pneumonia, septic infections, typhoid, tuberculosis, etc., which in many instances are only intercurrent affections. The question naturally arises, what are these very large spleens due to and are they suitable cases for splenectomy? It has yet to be decided what proportion of the cases dying from intercurrent diseases are due to pathological processes that would have terminated in cirrhosis of the liver and ascites if life had been prolonged. The comparative rareness of kala-azar in Burma negatives the possibility of this disease being responsible for the production of cirrhosis of the liver as a sequela in that country, and we have already shown in the Bombay series that although malaria is common, cirrhosis is very rare.

We are driven to the conclusion that, if we are to be guided by these groups of post-mortem findings, many of the largest examples of splenomegaly cannot be regarded as post-malarial or post-kala-azar conditions. It is possible that other causes or combinations of causes will be found to be responsible for their production.

The question very naturally arises, why is splenectomy performed so infrequently in India when splenomegaly of the splenic-anaemia type is comparatively common? The undoubted reason is the high mortality of the operation due to the miserable condition of low resistance in which the patients are admitted into hospital. Death is commonly due to shock within a few hours of the operation, or to broncho-pneumonia within a few days. This is well recognized in Egypt where the experience of surgeons of the one definite type of 'Egyptian splenomegaly' is very considerable, and yet with all possible precautions the mortality rate is over 20 per cent. In India and Burma in a very incomplete series of cases of splenectomy for splenomegaly of different types performed at various hospitals during the last ten years, the mortality worked out at 39 per cent. These operations were in some instances performed as a last resource, and the spleens were much enlarged with extensive adhesions. It is obvious that better results can only be obtained by operating at a much earlier stage, or by some different method.

In conclusion it can be stated that the evidence produced here is in favour

of the view that a large class of cases of considerable enlargement of the spleen, sometimes of doubtful aetiology, exists in tropical and sub-tropical countries. Many of these cases progress to a fatal issue in spite of therapeutic measures, and it is believed that some of them could be saved by surgical intervention. More light is needed to be thrown on the subject to facilitate diagnosis, and more experience is needed as regards preliminary treatment to raise the patient's resistance before operation. More exact methods are required, by radiography or otherwise, to determine before operation the extent of adhesion of the spleen to other structures; and improved technique is called for to deal successfully, by the removal or destruction, with a spleen bound down by many adhesions. Ligature of the splenic artery has been carried out with successful results in cases where the spleen cannot be removed; this manoeuvre is worthy of more extensive trial, particularly in the tropics when patients are often too debilitated to stand a more severe operation.

Summary

(i) This paper deals with splenectomy in the tropics, with special reference to tropical splenomegalies.

(ii) A more detailed knowledge of the pathology is needed, and better surgical technique; this can only be obtained by closer collaboration between the pathologist, physician and surgeon.

(iii) Reference is made to the incidence and treatment of ruptured spleens in India, and also to wandering spleen, abscess, cysts, and new growths.

(iv) Three groups of post-mortem cases are described, from Bombay, Calcutta and Rangoon, comprising 1,200 cases of enlarged spleen in 3,308 necropsies; a comparative table is given.

(v) One important class of very large spleens, resistant to treatment, stands out; this may terminate in cirrhosis of the liver and ascites. Some of these are thought to be malarial in origin. Splenectomy is indicated for some of this group.

(vi) Splenectomy has fallen into disfavour in India because of the high mortality rate. It is suggested that good results may be obtained with much less risk by ligature of all the branches of the splenic artery.

REFERENCES

- Chevers, N. (1870). *A Manual of Medical Jurisprudence for India*.
 De, M. N. (1932). *Indian Journ. Med. Res.*, Vol. XIX, p. 1029.
 Hughes, T. A., and Shrivastava, D. L. (1931). *Ibid.*, p. 565.
 Shanks, G., and De, M. N. (1931). *Ibid.*, p. 457.

[Note.—This address by Sir Frank Connor opens up a very important question. In our experience at the School of Tropical Medicine we encounter a large number of cases of splenic enlargement in which the blood picture is that of 'splenic anaemia'. The

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SEX HORMONES OF FEMALES

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THERE has been a very rapid development in the field of research work on the female sex hormones during the last few years. The whole problem is very intricate and necessarily a study of it is of great interest. In the following pages it is my endeavour to give a brief résumé of the researches and work that have been done on the sex hormones of the female.

History of hormonology

Professor A. A. Berthold of Göttingen, in 1849, first demonstrated, by means of experiment, the nature of activity of a true ductless gland. He showed that after castration of cockerels the typical appearances of the castrate are prevented by a reimplantation of the testicle. Claude Bernard is generally credited with having been the first to give expression to the doctrine of internal secretions in 1855. He maintained that, not only the glands by their secretory processes—*sécrétion externe*—by means of which substances are withdrawn from the blood, but that every organ of the body, by a process of *sécrétion interne* whereby it yields its products up to the blood, determines the composition of the blood and can, under certain conditions, modify and even change it.

But the actual introduction of the theory of internal secretions is universally ascribed to Brown-Séquard (1817—94), a native of Mauritius, whose life-work was mainly associated with French Medicine. He was the first to express the idea that all glands, with or without

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majority of these patients have suffered from both kala-azar and malaria, or from malaria alone, but parasites are not found in their peripheral or spleen blood, and specific treatment causes no improvement in their condition. They are often not acutely ill, but the prognosis in such cases is very bad and they remain in a chronic state of ill health for a year or so, and then die of some intercurrent disease.

We have recommended the removal of the spleen in a number of these cases, but we have no records of this having been carried out. The co-operation which Sir Frank advocates must also include that of the patient, and in our experience this has been the main stumbling block.

From two separate sources, both of which we consider unprejudiced and reliable, we have obtained two diagonally opposed opinions on the results of spleen removal in these cases. One physician said that in his experience in all of about a dozen such cases the patient had died of concurrent disease within a few years, though some had shown considerable temporary improvement; this did not reflect on the skill of the surgeons, because the deaths had not occurred immediately. The other, also a physician, said that he had often seen considerable and continued improvement following splenectomy in cases of this nature. Whichever view is accepted it is obvious that, when 'medical' measures have failed, surgery should be given a trial in suitable cases as there is no suggestion that the condition of these patients is worse after the operation, that very thorough investigation of the blood picture should be made prior to the operation, and, what is possibly even more important, that the cases should be followed up very carefully for a number of years, to ascertain the final result of the operation.

In addition to the causes which Sir Frank enumerates it will be recalled that some years ago Mackie (*Indian Med. Gaz.*, 1925, Vol. LX, p. 71) described the occurrence of a familial type of splenomegaly affecting several families in a village in the Bombay Presidency.—EDITOR, *Indian Medical Gazette*.]

ducts, supply to the blood substances which are either useful or essential, and the lack of which may produce pathological signs. The actual date upon which the doctrine of the internal secretions may be said to have been born is June 1, 1889. It was the occasion of that memorable meeting of the Société de Biologie, Paris, when Brown-Séquard, then 72 years of age, described the experiments which in order to prove the hypothesis, he had carried out upon his own person, by the subcutaneous injections of testicular extract.

Our present knowledge of the physiology of the female reproductive organs was initiated by Knauer, who in 1896 showed in experimental animals that transplantation of ovaries prevents the atrophy of the uterus that follows ovarian extirpation. This experiment as well as those of Hallan (1900) and of Simon (1904) proved beyond contention that the ovary is an organ of internal secretion.

What is a hormone?

'Two agents are concerned in the maintenance of the complex activity of the animal organism. In addition to the nervous inter-communication, there is also a "chemical correlation" of the different organs. In accordance with the latter, each organ, each tissue, each cell by means of its specific secretory products, acting through the agency of the blood stream, is capable of exerting a definite influence upon other parts of the body' (Biedl). Bayliss and Starling proposed that the name 'hormone' should be given to those physiological substances which act as 'chemical stimuli' and serve as intermediaries between different parts of the body. The word 'hormone' is derived from a Greek word meaning to awake or to excite. And organs producing such substances are called, 'hormone-producing'. The true hormones have been variously classified according to the manner in which they act. Thus we have formative and protective, growth-producing and growth-retarding, stimulant and inhibitory.

Hormones of the ovary

From the standpoint of endocrine physiology, the ovary must be considered a double gland. The follicular apparatus with its hormone folliculin constitutes the female sex gland proper. The corpus luteum with its hormone progesterin is an accessory gland concerned with pregnancy. Corner has proved conclusively that there are two hormones in the ovary, the one of the follicle he called œstrin, a growth substance having its specific influence during the proliferative stage of menstruation, the other of the corpus luteum he called progesterin, having the specific function of sensitizing the uterine mucosa for nidation of the ovum, and maintaining the raised nutrition of the uterus during pregnancy. These two hormones, œstrin and progesterin, are antagonistic to each other in their effects on the uterus but at the same time they are synergistic, i.e., they produce by combined action an effect which neither could effect when acting alone. Hisaw and Leonard explain the situation thus, 'The function of the follicular hormone seems to be that of putting the uterus in the proper physiological condition so that it can respond to the corpus luteum hormone. Neither of these substances can produce pregestational proliferation in the castrate uterus when given alone; if, however, it is brought into condition typical of œstrus through the injection of the follicular hormone, and is followed immediately by corpus luteum treatment, pregestational proliferation results'. Folliculin injections after impregnation prevent nidation of the ovum and produce abortion, whereas an excess of luteal hormone prolongs the term of gestation and may result, according to Brouha, in intra-uterine death of the foetus due to failure of the onset of labour.

Thus the seeming paradox of the two hormones, working both for and against one another, will be clearly understood by the above facts.

Recent researches show that the corpus luteum contains two hormones, lipamin, which promotes the

growth of the uterus and luteo-lipoid, which checks menstruation. The fully developed corpus luteum regulates the premenstrual changes, the growth of the decidua and of the musculature of the uterus, arrests ovulation in the early months of pregnancy and provides for the undisturbed development of the fertilized and embedded ovum.

The main site of production of the folliculin (œstrin) is in the unruptured Graafian follicle. It is also produced by corpus luteum and placenta. All evidence favours the view that 'atretic follicles' too produce the hormone and that it plays a large rôle in keeping up the trophic nutrition of the genital tract. It is found in amniotic fluid, and in the cord-blood and liver of the foetus. Mazer and Hoffman have found varying quantities of œstrin in the urine of pregnant women as early as the first week after the first missed period. It has been obtained from the blood, urine and bile of males; as well as from sex organs of higher plants, yeasts and in potatoes and other vegetables.

Progesterin (lutin) is elaborated only by the corpus luteum.

Thus, the two clearly defined endocrine activities of the ovary, due to two distinct hormones, occasionally become unbalanced as the result of overactivity of one or the other hormone. The disequilibrium often accounts for sexual disorders such as suppression or abnormality of the sexual cycle and for gestational disorders such as sterility, abortion and abnormal prolongation of the period of gestation. The ovaries differ from other endocrine organs (with the possible exception of the pituitary) in that their functional activities are cyclical. The hormones secreted vary in character and amount with the different phases of sexual activity.

The two hormones of the ovary have been called by a variety of names; that of follicle is known by œstrin, folliculin, female sex hormone, feminin, etc.; the corpus luteum hormone is called lutin, progesterin, beta factor, etc.

Hormones of the anterior lobe of pituitary

According to Zondek the anterior lobe of the pituitary elaborates the following substances:—

Prolan	{	1. Growth hormone.	} Super-ordinated sex hormones.
		2. Prolan A follicle-ripening hormone.	
		3. Prolan B luteinizing hormone.	
		4. Metabolism hormone.	

It will be seen that prolان A and folliculin have properties in common, while prolان B and the corpus luteum hormone, progesterin, are similar; hence prolان A and prolان B are known as superordinated sex hormones.

We know that there exists an inter-relationship between the various glands of internal secretions of the body, but that between the ovary and the anterior lobe of the hypophysis interests us only. The precise way in which the two ovarian hormones and the anterior pituitary hormones act and react upon one another is not yet clear. Just as the gonads are inactive in the absence of the anterior lobe, so the latter organ is incapable of promoting sexual changes in the absence of the gonads.

According to Zondek, prolان A sets off follicle ripening and incites in the theca cells of the follicle = the production of folliculin, which in turn induces the proliferative stage of the endometrium. Prolان B effects the change of the granulosa and theca cells and incites in them the production of progesterin (lutin) which changes the proliferative phase of the endometrium to one of the secretion (premenstrual, pregestational stage).

The placenta and its hormones

The placenta is becoming more and more regarded as a 'ductless gland of pregnancy'. It is both a store-house and a producer of substances necessary for the

nourishment and growth of the foetus. It contains among other things folliculin and an 'anterior lobe hormone'. It has been proved that the placenta actually elaborates folliculin. As to whether the so-called 'anterior lobe hormone' found in the placenta is stored there, its original source being in the hypophysis, or whether the placenta assists the hypophysis in supplying the extra amount required during pregnancy, or whether the placenta alone furnishes it, there exists at the present moment a controversy. Some, notably Phillip, hold that it is the product of the placenta. Zondek on the other hand claims the supremacy of the hypophysis.

Next we may discuss the effect of these researches on the modern conceptions of the onset of puberty, menstruation, parturition and lactation.

Phillip Smith as well as Zondek and Aschheim have demonstrated that the onset of puberty is an anterior lobe pituitary effect. As a result of this pituitary activation, a sudden increase and speed of follicle-ripening take place. Complete maturation of, at least, one follicle occurs with rupture and consequent ovulation, resulting in corpus luteum formation. If no pregnancy has taken place, after a short period, the corpus luteum involutes and regresses, ultimately forming a corpus albicans. If pregnancy has taken place the corpus luteum persists till the end of pregnancy. This fact has, however, merely changed the point of inquiry because no explanation is offered as to why the pituitary at this time suddenly increases its activity. As a passing remark it may be mentioned here that puberty can occur without the appearance of menstruation.

New theories of menstruation

The Graafian follicle as it develops produces by means of its hormone (folliculin) characteristic changes in the endometrium whereby the glands, at first simple tubular, become hypertrophied and tortuous. Near the middle of the menstrual cycle the follicle bursts, ejects the ovum and becomes a corpus luteum. The corpus luteum functions up to the 28th day, inducing by means of its special hormone changes in the endometrial glands by which their structure is altered to that of a secreting organ. The epithelium assumes the beaker form of secreting cells, and the glands exhibit a saw-toothed appearance. These changes become manifest as soon as the corpus luteum is formed. The ovum, if unfertilized, dies supposedly on the 28th day; with the death of the ovum the corpus luteum degenerates and menstruation supervenes. Here also it is not known why the anterior pituitary should produce this follicle-ripening material at a fluctuating rate. For the explanation of this extremely complicated problem Professor Dodds remarks, 'The modern German writers have developed an interesting theory but here a word of warning must be given that it is purely speculative. It is assumed that the anterior lobe pituitary begins to secrete prolan which in turn stimulates the ovary to secrete oestrin. Through the prolonged action of prolan, a corpus luteum is formed and in time this corpus luteum begins to secrete progesterin. The progesterin then reacts on the anterior lobe of the pituitary and reduces the secretion of prolan so that the corpus luteum retrogresses. When the corpus luteum has retrogressed we get an immediate re-establishment of the secretion of prolan, and thus the process goes on. It is not very difficult to think out some very serious arguments against this otherwise highly attractive theory. For example, it will not explain the enormous production of oestrin and prolan during pregnancy when presumably the corpus luteum is also continuing to secrete progesterin'.

Sex hormones and their relation to pregnancy and parturition

If after the extrusion the ovum becomes fertilized, the collapse of the corpus luteum and endometrium does not take place. The corpus luteum grows larger

and continues its hormonal influence on the endometrium. The endometrium persists as a secreting organ, becoming the decidua and retaining as such the characteristics of its premenstrual stage in a more pronounced form. Aschheim and Zondek found that in early pregnancy there is a relative excess of the anterior lobe pituitary hormones over the ovarian,

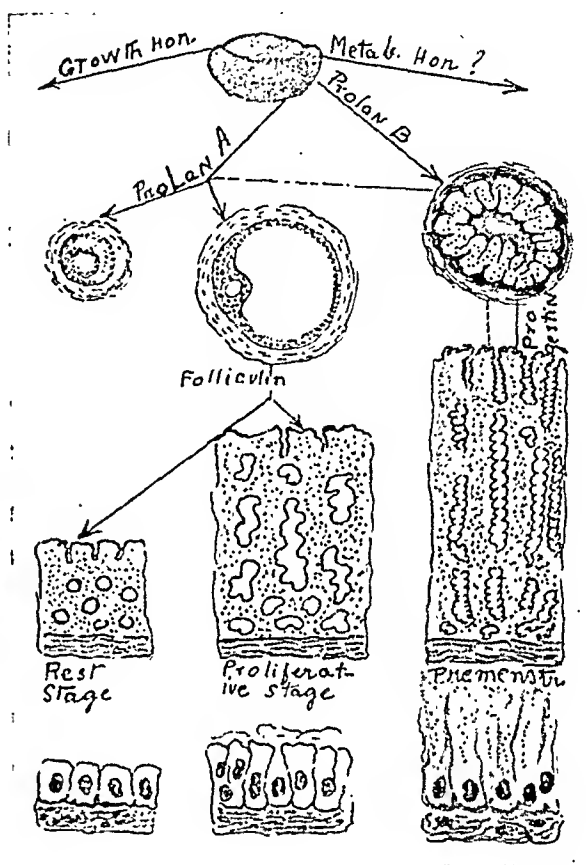


Figure showing the inter-relationship between the anterior pituitary and ovary and also correlation between ovarian and endometrial phases (after Zondek). Prolan A incites the ripening follicle to the production of folliculin, which in turn acts on the endometrium producing proliferative changes. (That corpus luteum also produces a small amount of folliculin is indicated by dotted lines.) Prolan B stimulates the corpus luteum to the production of progesterin which changes the proliferative stage of the endometrium to premenstrual stage. Under the influence of the ovarian hormones the endometrial glands, at first simple tubular in the resting phase, become saw-toothed and tortuous in the premenstrual stage.

whereas this position is reversed in the later months. It has been suggested that this change in the hormonal balance is probably concerned with the onset of labour. Jeffcoate has recently shown that if this upset occurs in the early stages of pregnancy then expulsive contractions of the uterus follow. Mention may be made here of the fact that a synergistic effect of folliculin and oxytocin, the oxytocic principle of the posterior pituitary, in stimulating the uterine contractions has been demonstrated and it has also been shown that administration of progesterin can make the uterus insensitive to this combination. Knaus has proved that there exists an antagonism between the internal secretion of the posterior lobe of the pituitary and that of the corpus luteum. It follows from this work that the action of the posterior lobe secretion in causing uterine

contraction is inhibited during pregnancy. Consequently, as postulated by Marshall, the regression of the corpus luteum is one of the main factors in bringing about parturition. Smith and Watkins remark, 'Just before delivery the outstanding endocrine situation is this:—folliculin has reached its highest level, the luteinizing hormone has decreased, and the corpus luteum apparently has become insignificant. With the disintegration of the corpus luteum, oxytocin acts on the uterus already sensitized by the œstrin and brings on labour'. It appears that oxytocin exerts its influence on the uterus only when it is first sensitized by the œstrin. Parturition normally occurs at what would have been a menstrual period if pregnancy had not supervened.

The explanation of post-maturity probably is that the progestin which normally holds œstrin in check is still being secreted in large quantities owing to non-disintegration of the corpus luteum.

Remarking on the new theories regarding lactation, Graves says, 'In some, it has been demonstrated that the proliferative and lactational changes of mammary glands during pregnancy and following parturition are due not to a follicular or corpus luteum hormone as formerly supposed, but to the direct action of the anterior lobe of the pituitary. Whether or not the effect is due to a special hormone of lactation or whether it is identical with one of the two proved hormones of the anterior lobe hypophysis has not been determined'.

Applied sex hormonology

Out of the researches have evolved various tests with modifications for the diagnosis of pregnancy. Of these, the one invented by Aschheim and Zondek is used universally with persistently uniform results. This test depends upon the presence of prolan B, the lutealizing hormone of the anterior lobe of the pituitary in the urine of pregnant women, which when injected produces characteristic changes in the ovaries of laboratory animals.

But substitution therapy has hopelessly failed to keep pace with the brilliant physiological discoveries in sex hormonology. In fact ovarian extracts have been used medicinally, for all kinds of menstrual disorders for a long time though without any success. It is only in very recent years that any attempt has been made to treat ovarian therapy scientifically. On the clinical uses of the ovarian hormones Marshall remarks, 'The use of œstrin is only indicated in cases where there is evidence of a natural deficiency of this substance as with certain types of amenorrhœa or after ovarian extirpation, and, much more problematically, at the time of the menopause. In a similar way the use of progestin may only at present be reasonably justified in cases where there is evidence of a deficiency of the hormone, if indeed this ever occurs. Such deficiency may conceivably be an occasional cause of abortion, but there is no direct proof of this happening'.

There are various commercial products of ovarian hormones in the market produced by commercial concerns for therapeutic uses, a list of which is appended below.

Preparations containing œstrin

Agomensin (Ciba), Amniotin (Squibb), Estrogen (Parke, Davis), Glovarian Pills (Schiefflin), Menformon (Degewop), Progynon (Schering), Theelin (Parke, Davis), Varium (Burroughs Wellcome).

Preparations containing progestin

Lipo-lutin (Parke, Davis), Lutein tablets (Hynson and Westcott), Sistomensin (Ciba).

The clinical results of these extracts have not been very promising and investigators all over the world have failed to obtain uniformly good results. This is due to the fact that effective sex hormone therapy depends on many factors among which the following are the most important, viz:—(a) proper biological assay and standardisation, (b) purity, (c) mode of administration. If the material is very active then it

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ACUTE PAINFUL CONDITIONS OF THE EAR

By K. E. MADAN, M.D., D.O.M.S.

Lahore

THE practical points in the differential diagnosis of the various acute painful conditions of the ear are not clearly mentioned in textbooks on the subject, and hence the following lines are meant to point out very briefly the important distinguishing features in their diagnosis. It is best to divide them into acute painful conditions of the external, middle and internal ear, and to referred pain in the region of the ear.

The diagnosis of acute painful external ear conditions, e.g., erysipelas, herpes, eczema, impetigo contagiosa, active hyperæmia, and other traumatic conditions is obvious or can be easily made out, so they will not be dealt with here. The acute painful conditions which affect the external auditory canal are (1) furunculosis, (2) inflammation, septic, diphtheritic, or pseudo-diphtheritic (croupous), (3) foreign bodies. The differential diagnosis of these and all other conditions

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must be given in a series of divided doses by subcutaneous injections. When administered orally, the hormones become inert. The water-soluble forms of the hormones undergo rapid deterioration with loss of potency. Also sometimes severe local reactions develop at the site of injection. Finally, the prices of these extracts are practically prohibitive.

SELECT BIBLIOGRAPHY

- Allen, E., and Doisy, E. A. (1923). *Journ. Amer. Med. Assoc.*, Vol. LXXXI, p. 819.
 Allen, E., Pratt, J. P., and Doisy, E. A. (1925). *Ibid.*, Vol. LXXXV, p. 399.
 Aschheim, S. (1927). *Arch. Gynäk.*, Vol. CXXXII, p. 179.
 Aschheim, S. (1930). *Die Schwangerschaftsdiagnose aus dem Harn*. Berlin: S. Karger.
 Biedl, A. (1913). *The Internal Secretory Organs. Their Physiology and Pathology*. London: John Bale, Sons & Danielsson, Ltd.
 Blair Bell, W. (1919). *The Pituitary*. London: Baillière, Tindall and Cox.
 Brouha, L. (1931). *Bruxelles Med.*, Vol. XI, p. 1479.
 Bugbee, E. P., and Simond, A. E. (1926). *Endocrinology*, Vol. X, p. 191.
 Corner, G. W., and Allen, W. M. (1929). *Amer. Journ. Physiol.*, Vol. LXXXVIII, p. 327.
 Dixon, W. E., and Marshall, F. H. A. (1924). *Journ. Physiol.*, Vol. LIX, p. 276.
 Dodds, E. C. (1928). *Lancet*, Vol. I, p. 1167.
 Dodds, E. C., and Dickens, F. (1929). *Journ. Obstet. and Gyn. Brit. Emp.*, Vol. XXXVI, p. 92.
 Dodds, E. C. (1932). *Proc. Roy. Soc. Med.*, Vol. XXV, p. 563.
 Evans, H. M., and Simpson, M. E. (1928). *Journ. Amer. Med. Assoc.*, Vol. XCI, p. 1337.
 Frank, R. T. (1929). *Female Sex Hormone*. London: Baillière, Tindall and Cox.
 Graves, W. P. (1931). *Female Sex Hormonology*. Philadelphia and London: W. P. Saunders.
 Halban, G. (1900). *Monatschr. Geburtsh. u. Gynäk.*, Vol. XII, p. 496.
 Jeffcoate, T. N. A. (1932). *Journ. Obstet. and Gyn. Brit. Emp.*, Vol. XXXIX, p. 67.
 Marshall, F. H. A. (1932). *Brit. Med. Journ.*, Vol. II, p. 232.
 Mazer, C., and Hoffman, J. (1931). *Journ. Amer. Med. Assoc.*, Vol. XCVI, p. 19.
 Parkes, A. S. (1929). *The Internal Secretions of the Ovary*. London: Longmans, Green and Co.
 Smith, M. G. (1927). *Bull. Johns Hopkins Hosp.*, Vol. XLI, p. 62.
 Zondek, B. (1930). *Arch. Gynäk.*, Vol. CXLIV, p. 133.

is made by the history, inspection, particularly with Siegle's pneumatic speculum, hearing tests, microscopic examination of the discharge, x-rays, and examination of neighbouring parts and comparison with the other ear.

As pain is a common symptom to all the acute conditions discussed here, careful attention should be paid in their differential diagnosis to note all the points regarding this important symptom of pain, such as its nature, degree, duration, location, extent, mode of onset, whether it is nocturnal or diurnal or continuous and which more severe in degree than the other, and whether aggravated by manipulations of the auricle, movements of the jaw, etc.

In *furunculosis* there is severe throbbing pain, and great tenderness. The pain extends to that whole side of the head and is aggravated by eating, due to movements of the jaw, and by even gentle manipulation of the auricle. Deafness is not complained of until the furuncle becomes big enough to close the canal.

In *acute diffuse inflammation*, there is early and intense pain, with deafness and tinnitus. The swelling of the canal does not allow a view of the drum-head. Over spots where the inflammation is greatest, there is some excoriation of the skin and a slight watery discharge.

In *diphtheria of the external auditory canal*, there is formation of a moist layer of pseudo-membrane which when pulled out causes bleeding. The Klebs-Loeffler bacilli are present in these membranes. In addition to pain, marked swelling of the meatus, deafness, and tinnitus, there are enlarged and tender lymphatic glands at the angle of the jaw with fever.

In *croupous otitis externa*, though a pseudo-membrane is present and when peeled off bleeds, the germs found are streptococci and staphylococci; the discharge is purulent and there is hardly any swelling of the neck glands.

Foreign bodies in most cases do not cause acute pain. If an insect is inside the ear, it ceases to give trouble as soon as it is killed.

Acute inflammation of the canal may also be produced by *otomycosis* which is due to fungus infection; although it is comparatively rare, it is a very troublesome condition. A moist, pasty, dirty grey, coloured mass occupies the entire canal, and pain, itching and stinging are complained of. This accumulated mass causes deafness. Microscopic examination shows the presence of *Aspergillus glaucus* or *niger*.

The tympanic membrane or drum-head may get acutely inflamed, a condition known as *acute primary myringitis*, due to some trauma, instrumentation, or action of irritating drugs or cold wind. In severe cases there are all the signs of acute inflammation, viz, pain, heat, redness, tenderness, swelling and loss of function resulting in a little deafness. Vesicles or even abscesses may develop in the dermal layer. Movements of the jaw, pressure in front of the tragus, or traction upon the auricle, increase the pain.

In *acute catarrhal otitis media*, the handle of the malleus is red with dilated vessels running across the drum-head, and the membrane is not quite as glossy as normal. When there is some fluid in the tympanum, a thin curved line is noticeable which represents the upper limit of the fluid. It is common to see air bells which shine and move on using the Siegle's pneumatic speculum. If no pultization air bells appear through the membrane, it shows the presence of fluid in the tympanum. In this condition also there is increased pain on jaw movements, pressure over the tragus, or outward traction on the auricle as in myringitis; but here in addition there is fullness and pain in the ear, deafness, tinnitus, and crackling sensations in the ear and vertigo in proportion to the exudate in the tympanum. Hearing tests show that there is deafness for aerial conduction, the lower tones being unheard but the medium and higher ones are heard. Rinnie's test is negative, and Weber's lateralization test refers

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THE MEDICAL PROFESSION AND THE BIRTH CONTROL MOVEMENT

By A. P. PILLAY, O.B.E., M.B., B.S.

Director, the Eugenic Clinic, Bombay

THE health of individuals and communities interests no class of persons more than the members of the medical profession and yet very few of us realise the great importance of birth control to these two subjects. Birth control, however, is primarily a problem of the woman and the two chief factors that greatly concern her are her own health and the health of her children. It will be conceded by every medical man that in certain physical and mental ailments, the woman should not conceive. If she does, she dies or her complaint is aggravated and the progeny is born debilitated or diseased. The maternity mortality rate in India is very high, ranging in places from 3 to 53 per thousand live births. The contention is not that all these deaths are due to the cause mentioned above but that it is a very important factor in a country where marriages are universal and the maternity service is notoriously crude. Add to this the thousands of mothers in India who are always ailing. It will also be conceded by the medical profession that adequate spacing of childbirths is essential in debilitated women in their own and in their children's interests. The following tables prepared by the Children's Bureau of the United States Department of Labour are interesting in this connection:—

Interval between births.			Infant mortality rate.
1 year	147
2 years	98
3 years	86
4 years	85

(Continued from previous column)

the sound to the affected side. Bone conduction is intensified. The patient hears his own voice sounds abnormally loudly in his affected ear, and those of others abnormally low as if coming from a great distance.

In *acute suppurative otitis media*, the attack is ushered in by shooting pain in the ear and side of the head, with temperature up to 103°F., deafness and tinnitus. The otoscopic appearances in the beginning are that the membrane becomes red and loses its transparency, and is bulged outward; the malleus handle may not be seen, but a dimple only may be found in its place; when perforation occurs, pain is relieved, and there is pus in the meatus and when this is wiped out, a minute perforation is seen; diagnosis is easier with Siegle's speculum; after cleaning the pus, if the hearing tests are normal, there is no otitis media, but some other condition like furunculosis or otalgia, in which carious or painful tender teeth, particularly molars, cause referred pain to the ear with tinnitus.

In *acute mastoiditis*, the first symptom is intense pain over the mastoid and the whole side of the head. The patient has a very anxious expression and has no sleep or inclination to take food. Fever, mastoid tenderness, sudden cessation of discharge from the meatus, swelling and congestion of the upper posterior part of the meatus are very significant of acute mastoiditis.

It should be kept in mind that the pain complained of in the middle ear, mastoid, and cerebral affections has the following distinguishing characters: in suppurative otitis media, pain is deep-seated in the ear; in mastoiditis, pain is behind the ear; in cerebral affections there is headache or the pain is in the head, and nocturnal pain is more severe; in the early stages of intracranial complications, when there is irritation of the dura, the pain is usually situated in the temporal region directly above the ear.

TABLE B

Number of children in the family.	Infant mortality rate.
4 and less	118
6 and more	267
7 and more	280
8 and more	291
9 and more	303

TABLE C

Order of birth.	Infant mortality rate.
1st and 2nd born	138.3
3rd and 4th born	143.2
5th and 6th born	177.0
7th and 8th born	181.5
9th and later born	201.1

TABLE D
(Indian figures)

	Infant mortality rate.	Percentage of stillbirths to live births.	Children alive per 1,000 pregnancies.
5 pregnancies and under.	226.3	12.5	633.7
6 pregnancies and over.	272.2	20.9	504.4

TABLE E

Age of mother.	Infant mortality rate.
Under 18	160.3
18—19	128.9
20—24	109.5
25—29	101.4
30—34	101.7
35—39	126.5
40—44	131.3
45 and over	250.0

The income of the family, it will be admitted, has a great bearing on infant mortality rate and the health of surviving children. The following table, again prepared by the Children's Bureau of the United States Department of Labour, is instructive:—

TABLE F

Earnings of father in dollars.	Infant mortality rate.
Under 400	170
450—549	130
550—649	120
650—849	110
850—1,049	90
1,050—1,249	70
1,250 and over	60

The infant mortality rate and the health of surviving children will thus be seen to be mainly dependent on:

- (1) The mother's health.
- (2) The child's possible heritage.
- (3) The father's earning capacity.
- (4) Child spacing and the number of children in the family.
- (5) The age of the mother.

Apart from the purely medical aspects of the question there are also certain factors coming under public health. Among these might be mentioned the following: birth control will lessen prostitution by promoting early and happy marriages and by allowing the husband to have all the sex life he needs at home without fear of injuring the health of his wife. It will also indirectly tend to reduce the incidence of venereal diseases. Overpopulation and its consequent evils like child labour and a low standard of living will be checked. This will leave the community free to raise its standard of health and living.

For controlling births and for child spacing there are at present only one unapproved and two approved methods. These are abortion, continence and birth control. Abortion no medical man worth the name will advise or practise, and yet the number of abortions that

are carried out or attempted every year even among the married, will run into lakhs. Any chemist, nurse or gynaecologist will confirm this statement from the number of entreaties they receive for prescriptions 'to regulate menstruation'. We are thus left with only two permissible alternatives, self control and birth control. To the medical profession there is nothing new in the statement that the sexual appetite, after hunger, is the most dominating and insistent instinct of life, though society, ignorant of the overwhelming importance of the subject, may clamour for its suppression. Self control implies the repression of a natural and necessary instinct and it is a psychological truism that repression of such an instinct is more harmful than its expression. Clinical data bear out this statement. Young and normal couples cannot long carry out this repression without mental, physical and moral deterioration. To those who can practise self control, the teaching of contraceptive methods is certainly unnecessary. My opinion is that most, if not all, physicians favour birth control and many practise it themselves. Why do they not then prescribe it in their practice? Is it lack of courage or lack of humanity or lack of knowledge of the subject? The reasons appear to be one or other of the following:—

- (1) Religious prejudice or conscientious objections of the doctors or their superiors.
- (2) Stigma of indecency.
- (3) Fear of its being misused.
- (4) Ignorance of the methods of birth control.

Science was once greatly dominated by religion but now it realises its power and value, just as it realises its limitations. This is why in treating and advising the sick, it does not allow religion to interfere. Advice on contraceptive methods is a form of treatment and why should religion be allowed to interfere in this case alone? Religion can lay down moral principles regulating the behaviour of individuals towards one another but it cannot meddle in the private affairs of persons. As regards the stigma of indecency there is none attached to the subject of birth control, or if there is any at all, it belongs to the mind of people who consider it indecent. Admittedly there is a possibility of birth control advice being misused, but then is it better that the world should go on being scourged with venereal diseases and with abortions and the sacrifice of countless mothers and infants than that it should be freed from these horrors at the expense *perhaps* of increased illicit sexual relations? To my mind, the chief reason why doctors do not prescribe contraceptive methods in their practice is their ignorance of the subject. They get their information not from specialists or from scientific treatises but from their friends who are often laymen, or from chemists' advertisements. This makes them doubt the reliability and harmlessness of the methods they know and hence they hesitate to prescribe them. Professor Julian Huxley says:—

'Our children will look back with incredulity upon an age in which doctors could warn women that they must on no account become pregnant again and yet withhold all advice as to how this could be accomplished, even when implored to give it'.

It is unprofessional, nay inhuman, to deny such advice to women who actually need it.

Sir Clifford Allbutt, when made President of the British Medical Association several years ago, said: 'Every righteous physician regards his practice as a social service, a means not only of bodily but also of social reconstruction and of moral and intellectual health'. The physician is hindered from this ideal by limitations as regards birth control which prevent him from acting to his fullest capacity as the adviser and guide in the processes of social reconstructions. This mentality is the cause of the subject of contraception being still in its infant stage and the rapid spread of unreliable and even harmful methods among the people. The medical profession can certainly be accused of adopting an unprofessional attitude towards this very necessary, humane and scientific subject.

Medical News

THE CALCUTTA HOSPITAL NURSES' INSTITUTION

(From *The Statesman*, 1st November, 1932)

NURSING PROSPECTS

A RESOLUTION published last week in the *Calcutta Gazette* states that in view of the burden thrown on provincial revenues by the cost of providing nurses in the general hospitals of Calcutta, the Government of Bengal have decided that the question in all its aspects should be investigated by a committee representative of the various interests concerned. The committee is to consider whether any economies can be effected by obtaining for their hospitals a supply of well-trained and competent nurses, male and female, from new local sources, without any lowering of the present standard, which looks uncommonly as if the Government, having given up the problem in despair, expect Colonel Stewart and his colleagues to square the circle for them.

There are in Calcutta, among other hospitals, the Presidency General, Medical College, Eden Maternity, Prince of Wales, Ezra, Eye, as well as the Carmichael Hospital for Tropical Diseases. All except the first-named belong to what may be termed the Medical College group, and all are Government hospitals. Under a rather unusual state of affairs the nursing staff for these hospitals are recruited, trained, and provided, free of charge, by an outside body, the Calcutta Hospital Nurses' Institution, which bears the whole cost of the food, clothing, pay, and servants of the nurses. Now these services cost money, and the necessary money is proving ever more difficult to find; hence the appointment of Colonel Stewart's committee. For their revenue the Institution depend principally on a Government grant; a small grant from the Corporation; donations from the charitably-minded public and firms of Calcutta, and to a limited extent only—a little over half a lakh of rupees in 1931—on fees from the hospitals. Expenditure in the year 1931 showed a trifling increase over the previous year, but did stand at Rs. 4,23,498 compared to Rs. 3,00,309 in 1921. Presumably the Institution's retort to the fact that expenditure between 1921 and 1931 rose by a lakh and a quarter of rupees would be that in the latter year the number of nurses maintained by the Institution, excluding superintending staff, stood at 236, compared with 178 in 1921.

On the other hand the Institution's revenue for the year 1931 showed a deplorable fall of Rs. 40,000. With two trifling exceptions every revenue head showed a fall, donations and subscriptions alone being Rs. 18,061 down on the year before. This is one tragic reflection of the world-wide depression, nor is it any comfort to learn that during the first half of the current year donations and subscriptions were Rs. 16,000 lower than during the corresponding period last year. Almost entirely because of this serious drop in revenue the Institution showed during 1931 a deficit of Rs. 42,928. In consequence new recruitment of nurses was closed as from December last, a step which was inevitable but which if prolonged cannot but result in heavy and increasing strain on the nursing staff and have deplorable results on the whole outlook for nursing in Bengal.

Is there any means for raising fresh revenues? Private donations and subscriptions, which stood at Rs. 1,54,366 in 1930, and Rs. 1,36,304 in 1931, constitute the Institution's principal source of income. Next come the Government of Bengal, who for some years have been contributing Rs. 1,25,000 annually, plus, from time to time, emergency grants. (Rs. 88,000 has been promised for the current financial year, for instance.) Private subscriptions not being likely, so far as one can tell, to show any increase for some considerable time to come, the Government remain the sole hope. But

Government complain that their revenue too has been dropping seriously, while demands on their resources are continually growing. This is the official reply to suggestions that Government's annual contribution should be increased to Rs. 1½ lakhs. Unless Government can come to the rescue a serious situation is inevitable. Estimates are notoriously difficult to make at the present juncture, but the Institution's income for 1932 is estimated at Rs. 80,000 less than it was in 1931, and the income for 1931 was Rs. 42,000 short of expenditure. As is the case in Bombay, several wards in the hospitals may have to be closed.

No fair-minded man can deny the difficulties facing the Government at the present time. Government have perhaps been slow to appreciate that certain hospitals are Government hospitals, and that however splendidly a hospital may be equipped with the latest technical apparatus the apparatus might just as well not be there if the nursing staff is inadequate, a state of affairs certain to prevail in the near future if the matter is not faced courageously as soon as possible. Government have also to consider their responsibilities to the taxpayer, European and Indian. It would be affectation to pretend that the nursing profession anywhere in India is regarded as it should be. In cases of serious illness the nurse may be more important than the doctor, but our correspondence columns during the summer showed a deep-seated reluctance on the part of the up-country and Calcutta public to appreciate this truism, as well as a strong resentment against any proposal that the standard fees should be raised. Some correspondents thought Rs. 10 per day or night ample remuneration in 'these hard times', forgetting that on the average nurses are occupied at most half the month, and that on this scale of ten rupees, even if a nurse were occupied the whole month, she would earn only Rs. 300. If that is the European and Anglo-Indian view, the Indian does not regard nursing as at all a profession in which to put his daughter. In fact, he very definitely regards it as something she should avoid. Until the public in India realize that for sick nursing, nurses are the most indispensable necessity of all, they must be prepared to see the health of the community suffer.

MEDICAL COLLEGE, CALCUTTA

DR. CHANDRA'S SCHOLARSHIP IN MATERIA MEDICA AND THERAPEUTICS

THE above scholarship of the value of Rs. 361-8-0 will be awarded during the session to the best candidate who complies with the terms of entrance for this scholarship, which are as follows:—

- (1) The scholarship is open to:—
 - (a) All senior students of the Medical College, Calcutta.
 - (b) Students at present studying at any medical college in India or Europe who have at any time been senior students at the Medical College, Calcutta.
 - (c) A graduate or licentiate in medicine who may have obtained either in Europe or in India a medical diploma or degree entitling him to practise medicine, provided that such graduate or licentiate at some time received a portion of his professional education in the Medical College, Calcutta.
- (2) Certificates to the effect that the candidate fulfils the above requirements, together with a certificate of good moral character, signed by a person of respectability, should be submitted to the Principal, Medical College, Calcutta, on or before 15th February, 1933.
- (3) Candidates will write an essay on the pharmacological action and therapeutic uses of *Rauwolfia serpentina* (dhan barua or dhan

marua), and submit this to the Professor of Pharmacology, Medical College, Calcutta, by 15th March, 1933.

Note.—Personal attendance is not necessary.

Preference will be given to the candidate whose thesis bears evidence of original investigation on the subject.

(The above is a résumé of the terms of the scholarship; for further details application should be made to the Principal, Medical College Hospital, Calcutta.—*Editor, I. M. G.*)

FIFTY YEARS AGO

(From the Editorial, *Indian Medical Gazette*, January 1883)

If future observation endows the germ theory with more substantiality than it now possesses, it will command very special attention and interest in the country, where so much sickness and mortality are due to

maladies which have repeatedly been attributed to microphytes, e.g., cholera, fever, leprosy, elephantiasis, syphilis and phthisis. Our knowledge of these diseases has not undergone any appreciable addition during the year, and it seems as if the mere study of the phenomena of these affections were insufficient to guide practice, whether preventive or remedial, and that until the intimate and immediate cause of them has been discovered, we must remain content to grope in the dark. It is remarkable and somewhat disheartening how little aid is derived from empiricism, and the history of medicine shows that this has ever been the case. If disease germs were indisputably demonstrated and their natural history thoroughly worked out, power would result from that knowledge, such as all the superficial and empirical labours of ages have failed to establish. One fact, however, of immense practical importance is yearly becoming more prominent, and that is, that, whatever the intimate cause of so-called zymotic disease may be, its dependence on sanitary shortcomings and prevention by sanitary reforms is indisputable.

Current Topics

Treatment of Hypertony

By I. HARRIS, M.D.

Königsberg

(Abstracted from the *Lancet*, 10th September, 1932, p. 560)

RECENTLY we have shown that the administration of certain drugs for the purpose of reducing pressure in cases of hypertony results in a disturbance of the equilibrium of the different blood constituents. Patients with hypertony whose pressure was reduced artificially showed an increase of blood-urea and non-protein nitrogen; the water-excretion function was depressed, the alkali reserve of the blood diminished, and the cardiac reserve power lessened. These facts suggest that the indiscriminate use of pressure-reducing drugs is extremely undesirable. In this paper an attempt is made to study certain methods of treatment of hypertony in relation to their action on blood chemistry.

At the outset it is necessary to differentiate between methods of treating hypertony whose object is simply the reduction of pressure without regard to ætiological factors, and methods whose aim is to reduce pressure by treating the causal factor. The first must be of doubtful value, the second can do nothing but good.

The patients were kept in bed. During the first week no treatment was given. During the second week Collosol sulphur was injected, 3 c.cm. daily. During the third week six pints of water were given daily. The patients were kept on a standard diet all the time. In other cases the procedure was altered. In the first week the patient had no treatment; in the second week he was put on salt- and sugar-free diet; in the third week a diet consisting mainly of carbohydrate, and in the fourth week a pure meat diet was given.

WATER

I know of no method of reducing blood pressure which is uniformly efficacious in all cases. Indeed, considering the various ætiological factors of hypertony, no uniformity can be expected. The drinking of large quantities of water effects a striking reduction in the blood pressure in many cases. I have used this method with good effect in cases of high blood pressure with a high degree of viscosity for the purpose of lowering the latter. At that particular time it was not clear to us why the action of water should have been what it was. I am now in a better position, I believe, to conjecture the reason of its beneficial action. I found

that in cases under sulphur treatment, *pari passu* with the reduction of pressure, there was an accumulation of deleterious substances in the blood. The same phenomenon was observed when the pressure fell simply as the result of heart failure. This suggests that high pressure in cases of hypertony is needed for the purpose of maintaining a normal chemistry balance in the blood. On the other hand, cases under treatment with water, although the blood pressure was definitely reduced, showed a normal blood chemistry. The beneficial effect of large doses of water is probably due to the fact that it enables the kidney to excrete urea and allied substances more easily. In this way a normal blood chemistry balance is maintained and there is no longer a necessity for a compensatory hypertony.

It has been contended that large quantities of water increase the strain on the heart by increasing the blood volume. It is, however, obvious that a treatment which reduces pressure and blood viscosity must also diminish the cardiac strain. Moreover, I have been able to show that there is no hydraemia after the imbibition of large quantities of fluid. Therefore there cannot be an increased blood volume under this treatment. So far as the kidney is concerned, the drinking of large quantities of fluid is all to the good. It has long been established that the work which the kidney performs in passing concentrated urine is far greater than when the urinary output is diluted.

SALT- AND SUGAR-FREE AND PROTEIN DIET

A salt- and sugar-free diet reduces and a protein diet increases the blood pressure. Broadly it may be stated that in hypertony the blood pressure stands in an inverse ratio to the non-protein nitrogen level in blood. It is true, as we have seen, that after the imbibition of large quantities of water both the pressure and the non-protein nitrogen (N.P.N.) tend to be lower, but in this instance the action of the water is what it is because it apparently does away with a causal factor of hypertony (*viz.* increased blood viscosity). The blood-urea is somewhat increased under the salt- and sugar-free diet and somewhat diminished under meat diet, although urea is an end-product of protein. It is possible that a low blood-urea after meat may be explained by the diuretic properties of this substance. The increase of blood-urea after a salt-free diet is by no means so pronounced and constant as it is under conditions where pressure-reducing drugs are given. It is possible the increase has something to do with the

this finding, it is generally considered that the endometrial change is associated with subnormal ovarian function. However, the complete removal of the ovaries does not lead to any similar condition, and J. B. Collip (1932) has found that the fluid from such follicular cysts in cases of this type of irregular uterine bleeding may contain up to 25 rat units of œstrin per c.cm. This suggests that there is a secretion of œstrin from the ovaries which is disproportionately great, whether absolutely or relatively to the reduced activity of luteal tissue which may be inferred from the appearance of the ovaries. With regard to the suggestion made by Shaw, that the ovary produces some abnormal toxic substance, it may be stated that similar suggestions have been made from time to time for other organs of internal secretion, but in every case the view that disturbances are due to excessive or deficient formation of the normal hormone has prevailed.

EFFECT OF THE HORMONE ON BLEEDING

Animal experiments show that excessive doses of œstrin not only affect the production of monophasic cycles, but in continued administration may eliminate the cycles. Excess œstrin affects the entire human organism. As regards the uterus the effect is not limited to the endometrium, but affects the myometrium as well, and herein lies an important consideration. The continued administration of moderate doses of the anterior pituitary-like hormone (A. P. L.) in immature female rats leads to the precocious appearance of normal œstral cycles, while the ovaries rapidly attain the size and appearance of those of normal adults. There is, therefore, reason to suppose that this substance might directly, or through the anterior pituitary, correct the changes observed in the ovaries in metropathia hæmorrhagica, and lead to the appearance of normal balanced ovarian function and the recovery of normal uterine structure and function. This expectation was realised in many cases of varied types.

Preparations of different strengths were used, but the dosage was so adjusted that the patient received at least 40 day-rat units per injection. Our best results were obtained by an injection every day for seven days, then every second day until the patient had passed through two menstrual cycles. When the menstrual flow became of normal duration and proportion treatment was discontinued. A high percentage of cases in all groups responded. In all groups there were some instances of recurrences of metrorrhagia or metrorrhagia, but upon reinstitution of the therapy the cases responded with comparatively few injections. Group D, however, proved disappointingly refractory.

In typical cases of so-called metropathia hæmorrhagica, the institution of A. P. L. treatment did not cause any immediate cessation of bleeding; indeed, while hæmorrhage commonly became less copious, there was no striking change for eight to ten days, and then the bleeding became very profuse, usually worse in the morning, with sharp 'spurts' throughout the day. This exacerbation, however, gradually subsided, and the bleeding practically disappeared except for slight metrorrhagia, for from four to five days' duration, or lasting into the next cycle. The majority of cases, when treatment was continued, manifested a menstrual period on the twenty-eighth day after the first exacerbation (which is regarded as an epoch superimposed on the background of more or less continuous hæmorrhage), and at this period the hæmorrhage was usually greater than a normal flow in duration and amount, clots and large mucosal fragments were passed, accompanied by considerable pain. Usually the treatment was discontinued at this point; if, however, the uterus remained large, and no pain was experienced, the treatment was continued; it was assumed with some reason that the bleeding of metropathia, which is characteristically painless, was not overcome and that the myometrium had not returned to normal. It may be that several menstrual cycles must elapse before the endometrial over-growths are completely shed, since Whitehouse has

shown that the uterine mucosa is not completely nor uniformly shed, even in normal menstruation. On the other hand, in cases which were curetted prior to the institution of therapy the result was considerably hastened. Once cycles of normal interval and proportion were established, they continued normally thenceforward, and in all cases which responded the uterus too returned to normal proportions. This maintenance of normal rhythm has been followed in some cases for over two years. There were, of course, exceptions to this typical history—for example, in women near the menopause, where the cessation of hæmorrhage is followed by amenorrhœa. It is of interest to note that the vasomotor disturbances of the menopausal syndrome did not appear in such cases.

In patients with continuous uterine bleeding dating from puberty the gross response was satisfactory, no matter how long the hæmorrhage had continued, though after one or two cycles the normal rhythm was not perfectly established, being punctuated with periods of amenorrhœa lasting up to three months. Only very occasionally did the symptoms recur. It is worth noting that over 10 per cent. of the cases in this entire series had at some time or another previously been treated with radium or x-rays, with only temporary improvement.

In cases of post-partum metrorrhagia the results were particularly good; there were ten cases treated, and all responded. Excessive menstruation following abortion responded similarly.

When pelvic inflammatory disease was the cause of metrorrhagia or menorrhagia the symptoms were aggravated by this method of treatment.

In cases of polymenorrhœa with flow of normal character, but recurring at irregular short intervals, it was sometimes possible to increase these intervals by three or four days; the previous condition, however, recurred when treatment was discontinued.

OTHER USES OF THE HORMONE

May I again emphasise the need of an outlook that extends beyond the endometrium and the study of mere local changes? The entire human organism is influenced by ovarian function. While the endometrium is a tissue easily accessible to study, the pattern of which alters from day to day, there are changes of a general biological character which may give rise to clinical symptoms, though they are not evident in the endometrial architecture.

In this connection clinical trial of A. P. L. extract was extended to other conditions. Thirty cases were treated for menopausal symptoms and 24 responded. The improvement was marked even when a considerable time had elapsed since the last menstruation. In six of these cases in which periods had ceased for various lengths of time up to one year, menstruation reappeared in from eight to ten days.

In cases with mastalgia, or so-called chronic mastitis, particularly those associated with abnormal menstrual cycles, not only was the pain relieved, but the small pea-like nodules in the breast disappeared. Let me add here that the normal mammary gland was never affected even in prolonged administration of A. P. L., nor was the post-partum breast in any way altered.

A form of urticaria associated with subnormal ovarian function and refractory to all other forms of medication disappeared with the administration of this hormone. Vomiting of early pregnancy was not improved, though it is worthy of note that in none of the cases treated was there any tendency to abortion. Cases of sterility, in most instances associated with polymenorrhœa, did not become pregnant, though two cases suffering from metrorrhagia became pregnant while being treated, and one other with a similar condition became pregnant immediately after cycles were established.

Dysmenorrhœa was intensified. It has previously been pointed out that in the treatment of menorrhagia and metrorrhagia the appearance of pain frequently

marked the beginning of improvement. Intermenstrual pain (Mittelschmerz) became more severe under treatment.

In cases with normal cycles no change either in the amount of haemorrhage or the duration of the interval was observed, even when the injections were continued for months.

A typical menstrual period occurred in ten cases of secondary amenorrhoea in from 10 to 14 days after therapy was instituted. No success was obtained in similarly treating primary amenorrhoea. The preparation of anterior pituitary-like hormone used by us did not cause any local symptoms or alteration in blood pressure levels or give rise to systemic reaction.

It is generally held that the corpus luteum is essential for normal menstrual cycles, but I believe that this dogma must be modified, as pointed out in a previous communication (Campbell and Collip, 1930). Moreover, Corner and Hartman have shown that the corpora lutea are not necessarily present in ovaries showing cyclic activity as manifested by menstruation. Ovarian function in the human may, therefore, be largely appraised by the regularity, amplitude, and duration of the menstrual epochs as well as by general well-being.

IMPRESSIONS

(1) There are several types of irregular uterine bleeding which may be distinguished by their menstrual histories. In selecting cases for treatment, correct diagnosis is essential; the organs in the pelvis must be palpably normal, and the presence of neoplasms of the uterus must be excluded. (2) Menorrhagia and metrorrhagia due to inflammatory diseases are aggravated. (3) Metropathia haemorrhagica responds particularly well. Pain is taken to signify that the musculature has returned to normal tone, and that the hyperplastic endometrium is being rapidly expelled. (4) Response is not so consistent in metrorrhagia of puberty, and treatment is followed by periods of amenorrhoea. (5) Menopausal symptoms are alleviated. (6) Mastalgia, if accompanied by disturbed menstrual cycles, frequently subsides. (7) No permanent improvement is noted in simple polymenorrhoea. The symptoms of dysmenorrhoea are intensified. (8) There is no effect in pregnancy, and no effect upon normal menstrual cycles as regards interval, amplitude, or duration; no local or constitutional symptoms are observed. (9) It is considered that the effect of the anterior pituitary-like hormone is to cause the ovary to resume a complete and balanced endocrine activity, in place of one that is unbalanced and incomplete.

The extract used in these studies was prepared in the Bio-Chemical Laboratory of McGill University by Professor J. B. Collip.

The End-Results of the Tonsil and Adenoid Operation in Childhood and Adolescence

By J. ALISON GLOVER, O.B.E., M.D., M.R.C.P., D.P.H.
and

JOYCE WILSON, M.B.

(Abstracted from the *British Medical Journal*,
10th September, 1932, p. 511)

1. THE rising flood of tonsillectomy has been shown in the immense and rapid increase in the numbers of operations annually performed, and by the astonishing fact that more than half the most carefully nurtured children in Britain are now subjected to it, whereas forty years ago none of their parents underwent the operation. Whilst the incidence of tonsillitis is at least as high amongst the poor as amongst the well-to-do, the children of the latter have an incidence of tonsillectomy at least four times as high.

2. A review of the literature suggests that, with the single exception of diphtheria, the incidence of the

ordinary infectious diseases is unaffected by tonsillectomy; that while the incidence of recurrent sore throats is perhaps somewhat diminished, that of frequent colds is unaltered, or perhaps slightly increased. The incidence of otitis and mastoid disease is the same, or perhaps slightly increased upon the tonsillectomized, while their liability to bronchitis and pneumonia is also probably slightly increased.

3. The evidence with regard to the prophylactic and therapeutic end-results of tonsillectomy on acute rheumatism, chorea, and carditis is distressingly confusing. There is no sufficient case for the routine removal of apparently healthy tonsils in a rheumatic or potentially rheumatic child, simply as a measure of prophylaxis against acute rheumatism. Removal should only be undertaken if there is some definite indication.

4. Observations have been detailed on the relative incidence of nasopharyngeal infections upon the tonsillectomized and the non-tonsillectomized pupils of a school population numbering nearly 14,000. Most of these pupils were between the ages of 13½ and 18, and belonged to the well-to-do classes. Save for two, with a total of 1,100 pupils, all the schools were boarding schools. Rather more than half of this population was tonsillectomized. Some of the observations cover a period of seven terms, or two and one-third years, whilst others are confined to certain terms of epidemic prevalence.

5. These interim observations (so far as they have gone) give no statistical support to the theory that the removal of tonsils closes an entrance for infectious or respiratory diseases. Hardly any cases of diphtheria have occurred, so that the prophylactic value of the operation in this disease could not be assessed. In scarlet fever, otitis media, and mastoid disease no significant differences were observed. In the two latter diseases the slight differences observed were in favour of the non-tonsillectomized.

6. These observations, based on actual *attack rates* in a school population, generally support the conclusions arrived at by Cunningham from a study of the *histories* of a similar number of somewhat older students. She found that the tonsillectomized pupils gave a history of higher incidence of all illnesses, and suggests that the fact that children who are often ill are those most frequently tonsillectomized may be the explanation. Comparing the proportion of the amount of illness reported before and after tonsillectomy in the same pupils, she suggests that the removal of tonsils had little influence in lessening the susceptibility to most infections.

7. We hold no brief for the retention of diseased or really obstructive tonsils or adenoids, nor do we wish to cast doubt upon the high value of the operation in cases in which there is sure evidence of toxic or obstructive damage. A review of the literature and the epidemiological observations made on a highly tonsillectomized child population suggest, however, that the excellent end-results of tonsillectomy in selected cases have been statistically overweighted by indifferent end-results in cases in which the operation has been performed without sufficient indications as a more or less routine prophylactic ritual. In our opinion, a large proportion of the tonsillectomies now done in children are not necessary, entail some risk, and give little or no return.

Error in Cancer Statistics

(Abstracted from the *Medical Press and Circular*,
New Ser., Vol. CXXXIV, August 31st, 1932, p. 157)

THE statistics heretofore published do not prove, according to Dr. K. Wolf, of Budapest, the assumption that the rate of mortality from cancer shows a rising tendency. A relative rise is the obvious corollary of the fact that the number of deaths from other curable and preventable diseases is diminished; but this means only that no defence against cancer exists because of ignorance concerning its cause, therapy, and its prophylaxis.

The average duration of life is steadily increasing everywhere, and cancer is the disease of old persons. If there are more elderly persons, more reach an age at which cancer is apt to occur. In Dr. Wolff's opinion the apparent increase in the incidence of cancer has been too much emphasised, for the mortality-rate of every disease shows oscillations, and the progressive rise in the incidence of cancer may be merely a natural oscillation. According to Dr. Zalka the error in the mortality statistics of gastric cancer is 31 per cent.; in uterine cancer 7 per cent.; in rectal cancer 19 per cent.; and in oesophageal cancer 130 per cent. His statistics, founded upon the necropsies performed upon patients over twenty years of age in the Budapest University Clinic, show a cancer-rate of 12.52 per cent. between 1919 and 1923, and he holds that these are more reliable than the older statistics. They show no progressive increase of cancer.

Radical Cure of Hernia: Regional Anæsthetic

By J. C. O. BRADBURY, M.B.C.S., D.M.C.P.

(From the *Practitioner*, Vol. CXXIX, No. 4, Oct., 1932, p. 510)

As a general practitioner of nearly thirty years' standing, faced with the operation of a radical cure for a right inguinal hernia of sixteen years' duration, I had to consider the choice of a general or local anæsthetic. Being somewhat subject to catarrh, though rather dubious whether I might move and interfere with the operator's work, I decided on the local and was backed up by the surgeon, Mr. Molesworth:—

In the morning I had a light breakfast and a cup of bovril at 10.30 A.M. My operation was fixed for 2 P.M. At 1 o'clock I had a hypodermic injection of omnopon gr. 1/3, scopolamine gr. 1/150, which in twenty minutes made me feel extremely confident of myself, and by the time I was in the operating theatre I felt somewhat drowsy, but knew exactly what was being done, and at the same time was most comfortable. The surgeon now began small intradermal injections of percain 1/1000 with a tiny hypodermic needle, this being a preliminary to the larger doses of the same which were given with a full-sized hypodermic needle and a large syringe. I had a slight pain when the deep muscles of the abdomen were injected, but this was really very slight. There was again some twinge of colic when the peritoneal sac was injected. I think the full time for the injection took from seven to ten minutes. I was now able to lie quite still whilst the whole of the operation was performed. The surgeon told me I should have a little pain while he pulled on the peritoneal sac and tied it off, but this again was very slight. I did not watch the operation, and was surprised when told that the skin incision was going to be closed.

I was away from the ward an hour, and it is true to say I did not have two minutes' pain or discomfort

whilst the operation took place. When I got back to bed I was quite comfortable, and after an hour had a cup of tea, but felt sleepy for three or four hours after, when the effect of the local anæsthetic began to wear off. I had little or no pain in the wound except when I coughed, when there was the usual tension on the stitches.

I may mention that I had the ordinary operation (Bassini's) and that the after-treatment of remaining in bed three weeks was carried out. Possibly this brief account may persuade others who are now enduring the discomfort of an ill-fitting truss to undergo the radical cure for hernia.

Aphorisms

(Abstracted from the *Medical Press and Circular*, New Series, Vol. CXXXIV, No. 4876, 19th October, 1932, p. 311)

WISDOM is the daughter of experience.—*Leonardo da Vinci*.

Nevertheless, I have always thought it a greater happiness to discover a certain remedy for even the slightest disease than to accumulate even the largest fortune, and whoever compasses the former I esteem not only happier, but wiser and better too.—*Sydenham*.

Living to old age 'goes in families'; and so does dying before old age.—*Pagel*.

Never believe what a patient tells you his doctor has said.—*William Jenner*.

The best physician is the most conscious of the limitations of his art.—*Benjamin Jowett*.

Every medical student should remember that his end is not to be a chemist, or a physiologist, or an anatomist, but to learn how to recognise and treat disease, to become a practical physician.—*W. Osler*.

Physical signs in the lungs are signs of physical conditions; their pathological significance is a matter of inference.

The special features of syphilitic eruptions are asymmetry and polymorphism.

All pyrexial states in old people are apt to set up a typhoid condition, because the kidneys are unequal to the task of depurating the blood.

In the typhoid state never use depressing antipyretics, e.g., the coal-tar derivatives.

A normal temperature may be present in diphtheria and pneumonia.

In typhoid fever occurring in children, the temperature may be normal or subnormal in the morning (hence the synonym 'infantile remittent fever').

Oedema of the chest wall in the presence of pleuritic effusion is a diagnostic sign of the effusion being purulent.

A high temperature cannot be relied upon to decide the diagnosis between inflammatory and malignant disease.—*A. T. Brand and J. H. Keith*.

Reviews

THE MEDICINAL AND POISONOUS PLANTS OF SOUTHERN AFRICA.—By Professor J. M. Watt, M.B., Ch.B. (Edin.), and M. G. Breyer-Brandwijk, Ph.D. doct. (Utrecht), Apotheker (Utrecht). Edinburgh: E. & S. Livingstone, 1932. Pp. xx plus 314. Illustrated. Price, Rs. 18-12. Obtainable from Butterworth and Co. (India), Ltd., Calcutta.

THE study of the indigenous drugs of ancient civilizations has attracted scientists for a long time. Many of the potent and efficient therapeutic remedies in the armamentarium of the modern physicians are the fruits of enquiry and investigation into the domain of the indigenous medicine of India, China and Egypt. African civilization was shrouded in darkness and mystery for

a very long time, and for want of authentic information on the medicinal plants of that vast country, scientists could not probe into the rich materia medica and folk-medicine of the Hottentots, Bantus, Bushmen and other native tribes of Africa. In the treatise under review, the authors have collected and systematised a mass of information on the medicinal and poisonous plants of South Africa. There is no doubt that the book will be of very great service to all those who are interested in the indigenous drugs of the country and will pave the way for further research and investigation.

The book will also be interesting to those who are working on the indigenous drug problems in India. Many of the 'natural orders' of South Africa are found

in abundance in India, and the description of the pharmacological and toxicological properties might be of help to workers in this field in India. The get-up of the book is excellent and the illustrations, both coloured and uncoloured, are beyond reproach. The bibliography at the end of each section shows that a good deal of time and energy has been devoted towards this side, though Indian workers would miss many references to important papers published in India. The indices of botanical names, common English and African names and active principles appear to have been carefully prepared and are conveniently arranged. The book should be kept in the libraries of all big educational institutions for purposes of reference.

R. N. C.

INDIGENOUS DRUGS OF INDIA: THEIR MEDICAL AND ECONOMIC ASPECTS.—By LIOUT.-COL. R. N. Chopra, M.A., M.D. (Cantab.), I.M.S., Professor of Pharmacology, Calcutta School of Tropical Medicine. Calcutta: The Art Press, 1933. Pp. 655. Price, Rs. 15.

THE publication of this unassuming, yet very important, book marks what we hope to be a very definite step forward in the progress of Indian medicine. It is the result of twelve years of intensive study of the problems involved and of very hard work by the author and his colleagues, much of which has been published in our columns. As Colonel Chopra has repeatedly pointed out, there are three main problems concerned; (a) the fact that many plants official in the British Pharmacopoeia grow in India, and that from these plants official B. P. preparations could be manufactured at a cost very much less than that now paid for the same articles when imported. *Digitalis* is a good example; the plant has been cultivated at Kumaon, Mungpoo, in Burma and in the Nilgiri Hills, and an official tincture can easily be prepared in India equal to the best imported stock at very much lower cost, and free from the very serious deterioration which this drug undergoes in transit through the Red Sea from Europe to India. (b) Secondly, many drugs equivalent to those official in the B. P. can be manufactured in India from plants indigenous in this country. *Ephedrine* is a good example; five species of this plant grow in northern India and yield an alkaloidal content quite equal to, even if not better than, the Chinese variety which now dominates the market. (c) Thirdly, it is worth while to investigate carefully the properties of those drugs in the indigenous systems of medicine in India which have an established reputation in the treatment of diseases, pharmacologically and clinically, to find out whether they are of therapeutic value or not. The author has been carrying out this work for the past twelve years, and the result is the introduction of such drugs as *kurchi*, and its alkaloid, *conessine*, in the treatment of amoebiasis, and of *kuth* root in asthma. Only by such careful and controlled investigation can the actual value of these drugs be assessed.

All these three factors enter into the making of this book, which one may regard as the precursor to an Indian Pharmacopoeia composed chiefly of indigenous drugs, prepared in India by indigenous drug manufacturers and sold at prices within the reach of the Indian *ryot*. To take another example, there seems to be no good reason to-day why India should export large quantities of tea dust to America, only to buy a good deal of it back as caffeine. Some idea of the expenditure of India on foreign drugs is given on pp. 21 to 24 of the book; thus the import of pharmacopoeial preparations and chemicals reached a figure of 114.3 lakhs in 1927-28, and that of proprietary and patent medicines a figure of 42.8 lakhs. Most of this expenditure is preventable, and its place could be taken by drugs of indigenous origin.

The book is divided into five parts. Part I deals with the medical and economic aspects of Indian indigenous drugs, and here a very interesting historical sketch precedes a general outline of the present position. Part II deals with the potential drug resources of India, taking up separately the pharmacopoeial and allied drugs, one by one. Part III deals with the drugs used in the indigenous systems of medicine, dealing separately with those of vegetable and those of mineral and animal origin. Part IV, 'Indian Materia Medica', must have involved an immense amount of labour in compiling. It commences with a list of references to the literature from 1810 to 1932, followed by one of journals consulted. Then comes a list of Indian medicinal plants, some 3,000 in number, with their vernacular names, their uses in the indigenous systems of medicine, chemical composition, and references to the literature. This list alone is quite unique, and will serve as a standard work of reference for many years. This is followed by lists of inorganic drugs and of those of animal origin used in the indigenous systems, and a miscellaneous section on remedies used in snake bite and scorpion bite, and of plants containing poisonous principles. Part V enumerates the common bazar medicines of India, giving full vernacular names in all languages, and indications for their use. Finally comes a very full and detailed index of common vernacular names, and a final general index.

No one could ask for any work more authoritative, more detailed, and yet more handy on the subject. The Indian medical practitioner and the Indian chemist will find here everything that he requires in the way of information, whilst the research worker will find full guidance to the literature on his subject. The book is not only timely in its appearance, it should meet a very long-felt want, and supplant much of the literature which is now so old and out-of-date. We cordially welcome its appearance and desire to bring it to the special attention of our readers.

A last word must be said in praise of the publishers. Paper, printing, and binding leave nothing to be desired, and in these respects the book is far and away above the standard of the ordinary medical book published in India. Both the author and his publishers are to be warmly congratulated on its publication.

R. K.

'MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS.'—By W. A. Bastedo, Ph.G., M.D., Sc.D. (Hon. Columbia), F.A.C.P. Third Edition. Reset. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 739. Illustrated. Price, 32s. 7d.

PROFESSOR BASTEDO'S book was very well received on its first appearance in 1913 and since then it has been a constant source of inspiration to students and teachers alike; this is evidenced from the number of reprints and editions it has passed through. Chemistry, physiology, pharmacology and the allied sciences have made rapid strides during the last two decades, and a large number of new remedies have been introduced into medicine and therapeutics. The recent edition of Professor Bastedo's book has been largely expanded, revised and rewritten wherever necessary, to cover every advance in these fields. The sections dealing with alcohol and *digitalis* have been brought up to date and are extremely interesting. Students will get all the newer knowledge with regard to insulin, ovarian hormones and their application in menstrual disorders, the hormones of the anterior pituitary, *ephedrine*, and drugs such as *plasmochin*, and dyes stuffs. The text on the whole is clear, instructive and accurate, and the book can be strongly recommended by all teachers to their students going up for university examinations.

R. N. C.

MATERIA MEDICA, PHARMACY, PHARMACOLOGY AND THERAPEUTICS.—By W. Hale-White, K.B.E., M.D. (Lond.), M.D. (Dub.), LL.D. (Edin.). Twenty-first Edition. Revised by A. H. Douthwaite, M.D., F.R.C.P. London: J. & A. Churchill, 1932. Pp. x plus 547. Price, 10s. 6d.

DR. HALE-WHITE's book was first published in the year 1892, nearly 40 years ago. Since then, the book has been reprinted several times and has passed through twenty editions. This speaks in no uncertain terms of the great popularity of the book among the students and teachers of medicine. It is not too much to say that wherever western medicine is taught and read, Dr. Hale-White's book is well known. Medical and allied sciences have made rapid progress during recent years and nowhere is the advance more evident than in the sciences of pharmacology, pharmacy and therapeutics. The great merit of Dr. Hale-White's *Materia Medica* is that it has always kept itself abreast of the modern developments and never failed to create a demand for itself with changing times. The reviewer read the book as a student, and as a teacher of the subject the book is still his constant companion.

The twenty-first, the edition under review, has been thoroughly revised and brought up to date by Dr. Douthwaite. The book has assumed a new garb and those who used the book before will miss the handy volume which they could carry in their pockets. The present edition is, however, quite convenient in size and has maintained the prestige of its predecessors to the fullest extent. On account of the publication of the new British Pharmacopœia, drastic changes have been effected in the list of drugs and their dosages; all these changes have been incorporated in the present volume. We have no doubt that this edition will be as popular as the previous editions.

R. N. C.

THE ELEMENTS OF MEDICAL TREATMENT.—By R. Hutchison, M.D., F.R.C.P. Second Edition. Bristol: John Wright and Sons, Ltd., 1932. Pp. 188. Price, 5s.

THE author of the present volume has written several books which have been a great boon to medical students and practitioners, and this work is no exception. In the 'Elements of Medical Treatment' the author has indicated the management of patients, and the dietetic and medicinal treatment of the common diseases met with in daily practice, in a clear, concise and lucid manner. The large demand for and the popularity of this book is evidenced by the fact that in the two years following its first publication it was reprinted twice and that a second edition had to be published a short time after. In preparing the present edition the author has largely rewritten and brought up to date the chapter on the treatment of anæmia and has added chapters on sedatives and physiotherapy. This book should be in the possession of all medical students working in the hospital wards and in the library of all junior practitioners.

R. N. C.

HEART DISEASE: THE PRINCIPLES OF DIAGNOSIS AND TREATMENT.—By C. Bramwell, M.A., M.D., F.R.C.P. London: Edward Arnold & Co., 1932. Pp. vii plus 244. Illustrated. Price, 12s. 6d.

MUCH has been written and said about the diseases of the heart and circulation, and the number of books on the subject is legion. In these days of specialisation, the tendency of most authors is to present a detailed and exhaustive treatise in which the subject is dealt with from all possible angles and where every detail is attended to. Dr. Bramwell has made no attempt to

cover the whole field of cardiology and has only endeavoured to illustrate the important general principles of the subject. To the advanced cardiologists and veteran research workers, therefore, the book may be found wanting in certain respects, but to practitioners who want to approach their cardiac cases intelligently, the book is sure to make a wide appeal. The book is written in simple and lucid language, and the accounts of the different conditions are particularly free from the ambiguous statements that are so commonly met with in books of this nature. The readers are not likely to lose sight of the main issues involved in a mass of detail which is more of theoretical than of practical value.

The modern outlook on heart disease has been admirably brought out, and stress has been laid on the ætiological factors concerned in its causation. The importance of the murmurs and valvular lesions has been rightly relegated to the background. A systolic murmur by itself alone has been stated to be of little or no consequence from the point of view of prognosis. The significance of the electrocardiographic tracings is very briefly mentioned. In view of the importance of this branch one would have expected a longer dissertation on the subject. The author has also not gone deeply into the question of treatment and drug therapy. In spite of these minor shortcomings the book will form a very useful addition to the library of medical practitioners in this country.

R. N. C.

CLINICAL ENDOCRINOLOGY OF THE FEMALE.—By C. Mazer, M.D., F.A.C.S., and L. Goldstein, M.D. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 519. Illustrated. Price, 30s.

THE endocrines have been the subject of a good deal of experimental and clinical research during recent years. Our knowledge regarding the part played by these glands has greatly increased and we are now in a position to utilise our findings in this field in practical therapeutics. Thus, the value of organotherapy in the treatment of menstrual disorders has now been placed on a definite footing, though scepticism still exists. The authors have been interested for many years in the endocrinology of the female sex glands and have presented the subject in an easy conversational style which will not fail to make a wide appeal to gynaecologists, clinicians and teachers. The book is replete with useful information for laboratory workers who will find it profitable to go through the chapter on the hormone tests for pregnancy. The agents employed in the treatment of disorders of menstruation have been set forth in detail. The indications and contraindications for the use of 'œstrin', the ovarian hormone, and 'progestin', the luteal hormone, have been given and the different forms in which these are available in the market for ready application to patients are recorded. Low dosage irradiation of the pituitary gland and ovaries as a therapeutic measure has also been discussed. The book, though of particular interest to the gynaecologist, will also be useful to the general practitioner. It should find a place in all medical libraries.

UROLOGY IN WOMEN.—By E. C. Lewis, M.S. (Lond.), F.R.C.S. (Eng.). London: Baillière, Tindall and Cox, 1932. Pp. 76. Illustrated with 21 plates and 4 figures in the text. Price, 6s.

THIS is a small volume of 76 pages, which the author states 'is not intended to be a complete treatise on urology but rather to emphasize certain points which have a peculiar application in women patients'. At the end of each chapter illustrative cases are given briefly. The chapter on the kidney is very good. The printing is admirable and the illustrations excellent.

S. A. McS.

ESSENTIALS OF SURGERY.—By M. L. Mitra, M.D., F.R.C.S. (Edn.). Volumes I and II. Second Edition. Calcutta: Scientific Publishing Co., 1932. Pp. vii plus 538 in volume I and 555 in volume II. Price, Rs. 12.

WHEN the number of textbooks on surgery is already so large, the only justification for adding to their number is the publication of a work which presents the subject in a novel way or which meets the needs of a special type of student. The second edition of the above volumes, admittedly not original, is specially written for the requirements of Indian medical students and closely follows the lectures of the author. The subject is presented with admirable clearness, emphasis being laid on tropical surgical conditions as well as the commoner surgical affections. While aetiology and pathology are given due share, clinical features and diagnosis receive full recognition, and treatment is eminently clear, practical, and, as is necessary in an elementary handbook for students, somewhat dogmatic.

The author is to be congratulated on producing one of the best of the many synopses that have been written; it will be found of great help to the student in revision and in preparing for examinations. The size is very handy and the get-up excellent. There are a good many printer's errors which it is hoped will receive attention in the next edition.

V. S.

ONE HUNDRED POPULAR FALLACIES.—By C. W. Budden, M.A., M.D., Ch.B. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. viii plus 162. Price, 3s. 6d.

DR. CHARLES BUDDEN is a refreshingly graphic writer. He succeeds by this means and through gentle ridicule in driving his points home without making more exaggerated statements than is permissible in articles intended for educational propaganda in matters connected with the people's health.

One Hundred Popular Fallacies was originally published as a series of articles in *Maternity and Child Welfare* and like all articles from Dr. Budden's pen appealed to so wide a public that a reprint in book form is justifiable. The fallacies dealt with are chiefly connected with maternity and child welfare, and range from superstitions so lacking in any foundation that it seems incredible they are still widely held in large areas of the country, to opinions which were at least countenanced, if not expressed, by the family doctor only a few years ago. Some of the fallacies judging from advertisements in the medical journals are, even in these days of enlightenment, popular with the medical profession. Such a belief is the one that thumb sucking can be cured by various appliances instead of by re-education and substitution of beneficial activities for this form of self-indulgence.

Dr. Budden's remark 'we have no use for tonsils' requires modifications perhaps, but the articles as a whole are full of wisdom and understanding, and the reprint makes a very readable book.

J. M. O.

AIDS TO BIOLOGY.—By R. G. Neill, M.A. London: Baillière, Tindall and Cox, 1932. Pp. vi plus 257, with 27 figures. Price, 3s. 6d.

THIS handbook of the Students Aid Series is designed to cover the syllabus of the 'Higher School Certificate' examination of Cambridge and other universities. The subject has been presented in a suitable form for students and the book will be particularly helpful at the time when rapid revision of the subject just before the examination is necessary. The chapters dealing with algae and fungi in section I, and the chapter on sex and heredity in section II are worth special mention. The different theories of evolution have been described

in a clear and concise manner. The complex processes of cell division, which are usually baffling to the beginners, have been illustrated and made interesting. The medical students doing biology in the Indian universities would find the book profitable reading.

PRACTICAL ANATOMY.—By Six Teachers. Edited by E. P. Stibbe, F.R.C.S. London: Edward Arnold and Co., 1932. Pp. xii plus 719. Illustrated. Price, 30s.

THIS book is intended to provide a complete course in practical anatomy to the students going up for the 2nd M.B., the conjoint board and the primary fellowship examinations, and has special features which are not commonly met with in many treatises of this nature. The production is the joint effort of six well-known teachers in the field of anatomy and the various sections have been dealt with by specialists in their particular branches and are rich in anatomical detail. A large number of new and original drawings, some of them very instructive, have been added, and the diagrams in the sections dealing with the orbit and the ear are worthy of special note. Although it is a practical guide, it would appear that the instructions for dissection are not so explicit and detailed as in some of the older books. The book can be strongly recommended to teachers and advanced students in this country.

ANATOMY. Part I. (Catechism Series).—By R. Whittaker, F.R.C.S.E., F.R.S.E. Fourth Edition. Revised and enlarged. Edinburgh: E. & S. Livingstone. Pp. 80. Price, 1s. 6d. Postage, 2d.

THIS small book of the Catechism Series deals with the anatomy of the superior extremity. The muscles and fasciae, the vessels and the nerves have been subdivided into those of the (1) shoulder and arm, (2) forearm, and (3) hand. The joints as well as the ossification of the bones of the whole extremity have been considered together. The relations of the important muscles and the main vessels have been well put. The only criticism that we can offer is that the scapular circumflex artery has been so placed that it might be mistaken for one of the branches of the third part of the axillary artery. The time of appearance of the epiphyses and their fusion with diaphyses are to be accepted with caution in view of the recent radiological observations. The book does not pretend to replace textbooks on anatomy, but is admirably suited for revision work and for refreshing the memory of the students before they sit for their examinations.

N. P.

A TEXTBOOK OF ANATOMY AND PHYSIOLOGY.—By J. F. Williams, M.D. Fourth Edition. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 601, with 416 illustrations, 32 of them in colours. Price, 14s.

THE new (fourth) edition of Dr. William's book will be enthusiastically received by students and teachers alike, of nursing, physical education, physiotherapy, and allied branches of practical arts. The interesting feature of the volume is its close linking of the two important and related subjects, without a good groundwork of which the education of no students in these branches is likely to be sound. Besides purely anatomical and physiological matter, elementary facts of embryology and pathology are given without needless discussion of intricate details. At the end of each chapter, practical exercises and questions are appended which are likely to stimulate the reasoning faculties of the students. The teachers will also be greatly benefited by the select references attached. The illustrations, though generally not coloured, are clear and expressive. The book is up to date in every section and the arrangement shows that the author has got great teaching experience.

Annual Reports

LEAGUE OF NATIONS, HEALTH ORGANISATION, EASTERN BUREAU. ANNUAL REPORT FOR 1931

THE Eastern Bureau of the Health Organisation of the League of Nations was established in order to collect and disseminate information of an epidemiological nature in the Far East more quickly than it could be done through Geneva or through the Office Internationale of Paris. The Bureau is located at Singapore. Information regarding outbreaks and incidence of epidemic disease is sent to the Bureau from Far Eastern countries and is quickly collected and sent by telegram and cable to countries and ports all over the Far East and to several ports and countries outside.

The Bureau also compiles an interesting and useful weekly fasciculus of the incidence of epidemic disease in the Far Eastern area. It also publishes an annual report. Dr. Gautier who has acted as Director of the Bureau since its inception has returned to Geneva and his place has been taken by Dr. Park late of the Australian Quarantine Service. The part played by Indian ports in the dissemination of disease in the Far East is well brought out in the report. Calcutta was the port in which cholera infection was contracted in the case of seven vessels out of 19 infected. Calcutta and Shanghai were the two ports from which smallpox infection was exported to the greatest extent.

Of the two vessels found infected with plague one would seem to have been infected at Rangoon. Bombay, Colombo, Rangoon and Bassien remained plague-infected more or less continuously throughout the year. An interesting feature of the report is the evidence of the increased part that the Republic of China is now prepared to play internationally in health matters. Dr. Wu Lien-Teh, already well known for his work on Manchurian plague, is the head of the new National Quarantine Service of China which is dealing particularly with cholera infection and dissemination. A distressing account is given of the floods in China in 1931, relieved by the descriptions of the assistance given by the organisations of various neighbouring and outside countries.

The Bureau has conducted research and liaison work in plague and cholera. The work of Asheshov and Morison on cholera bacteriophage is reviewed and its possible implications pointed out.

The Bureau is destined and fitted to play an increasingly interesting and useful part in the prevention and control of infectious disease in the Far East.

REPORT OF THE EUROPEAN MENTAL HOSPITAL, RANCHI, FOR THE YEAR 1930. BY LIEUT.-COL. O. A. R. BERKELEY-HILL, M.A., D.M., I.M.S. RANCHI: SUPERINTENDENT, GOVERNMENT PRINTING, BIHAR AND ORISSA

THIS annual report is always a most interesting one. The following abstracts from it will serve to summarize it:—

Accommodation.—The accommodation of the hospital during the year under report remained the same as in the previous year, *i.e.*, for 106 males and 100 females or a total of 206 of both sexes.

Summary of notable changes.—There have been very few changes or innovations to record during the past year. I would like to record the acquisition of portraits of the famous men after whom our wards have been named. First we have to thank Dr. Henry Yellowlees, O.B.E., M.D., of the Retreat, York, for a present of a fine portrait of the humane William Tuke, the founder of that institution. Then we have to thank Dr. Lange of the Psychiatric Institute at Munich, for presenting us with a portrait of the late Professor Emil Kraepelin,

to be placed in the ward named after this great German alienist. Then our thanks are due to Dr. Daniel, Medical Superintendent of Hanwell Mental Hospital, for presenting us with a photograph of the portrait of Dr. John Conolly, the first English alienist who tried to abolish the habitual cruelty with which the treatment of the insane was notorious up to the end of the 18th century. The photograph was enlarged very successfully so that patients, staff and visitors to the hospital can now gaze upon the handsome face and figure of that pioneer in English psychotherapy. I have also to thank my friend, Dr. Edward Mapother, Medical Superintendent of Maudsley Hospital, for his kindness in permitting me to have a reproduction made of the portrait of Dr. Henry Maudsley that hangs in the hall of the hospital he founded and endowed in London. Portraits of William Cullen and Giovanni Battista Morgagni have also been obtained and they now decorate a wall in the ward named respectively after the great Scottish and Italian reformers of psychotherapy. So far we have failed to obtain portraits of Philippe Pinel and Juan Gilaberto Joffre. For the hospital not yet to possess a portrait of Pinel, the greatest of all the opponents of cruelty to the insane, is very much to be deplored, for Philippe Pinel was the first to adopt, in face of much opposition, an attitude of kindness and sympathy in dealing with the mentally disordered. Further, and this is a point that should never be forgotten in the Ranchi European Mental Hospital, the first patient in the Salpêtrière hospital in Paris, whom he selected for more humane treatment, was an Englishman, a sea captain, who had lived in fetters for no less than forty years. It is pleasant to think that this fierce and powerful madman repaid the wisdom and sympathy of Pinel by henceforth constituting himself the protector of the lion-hearted little doctor from any possible risk of assault that he might have run through suddenly liberating patients from the chains which, combined with many other forms of cruelty, had rendered them both violent and dangerous to the staff of the hospital whom they naturally regarded as their persecutors.

The maximum number of patients resident in the hospital on any one night was 213 (106 males and 107 females) against 206 (106 males and 100 females) in the preceding year.

The number of patients resident in the hospital at the beginning of the year under report was 101 males and 103 females or a total of 204 of both sexes as compared with 193 in the previous year.

The admissions (including re-admissions) during the year under report were 78 (37 males and 41 females) as compared with 62 (35 males and 27 females) in the previous year.

The total population of the hospital for the year under review was 282 (138 males and 144 females) against 255 (125 males and 130 females) in the previous year.

The daily average number resident in the hospital during the year under report was 200.61 (99.90 males and 100.71 females) against 199.51 (97.45 males and 102.06 females) in the preceding year.

Percentage of cases 'cured' and 'improved' to daily average strength.—The annexed table shows the ratio per cent. of cases 'cured' and 'improved' to daily average number resident in the hospital during the year under review as compared with the preceding year:—

Cases		1930	1929
Daily average number resident in the hospital	200.61	199.51
Ratio per cent. of cases—			
(a) Cured	9.91	5.95
(b) Improved	22.43	8.57
TOTAL		32.34	14.52

It is satisfactory to note that the number of patients discharged as 'cured', shown in the above table, is considerably higher than that recorded in the previous

year. It is of further interest to note that such patients are all new admissions. Also, it will be noted that the number of cases shown as 'improved' during the year under report is considerably higher than in the previous year. The reasons assigned to this satisfactory state of affairs are mainly two—first, improvements in every direction in therapy which have followed upon the increase in experience among the medical and European nursing staff, and secondly, the necessity that has arisen to keep the waiting list of applicants for admission as small as possible in view of the great importance of early treatment in all forms of mental disorder.

Percentage of cases 'cured' and 'improved' to direct admissions.—The table appended below gives comparative data relating to percentages of cases 'cured' and 'improved' to direct admissions during the last two years:—

	1930	1929
Total population	282	255
Compare—		
Direct admissions	78	62
(a) Ratio per cent. of cases 'cured' to direct admissions	20.51	12.90
(b) Ratio per cent. of cases 'improved' to direct admissions	21.79	20.97

Distribution of period of hospital life of patients discharged cured.—The distribution of periods of hospital life of those who left 'cured' during the year under report and in the previous year is shown in the annexed table:—

Period	CASES		
	1929	1930	Total
Under two months	5	6	11
Over two months and under four months	3	10	13
Over four months and under six months	2	2	4
Over six months and under eight months	1	1	2
Over eight months and under one year	1	..	1
Over one year	1	1
TOTAL	12	20	32

The figures in the above table indicate that if patients in the early stages of mental disorder are properly treated in a mental hospital, they have a good prospect of early recovery.

Death-rate.—The death-rate calculated on the average number daily resident in the hospital during the year under report was 6.92 which compares favourably with 7.05 in the preceding year.

Among the patients who died, there was one male who died of rupture of the spleen as a result of injury inflicted by another patient, and one female who suddenly died of suffocation in the ward during an epileptic fit.

Bodily ailments.—The daily average number of cases treated in the hospital for bodily ailments was 5.45 as compared with 0.39 in the previous year, giving an increase of 5.09. The large increase in the proportion of admissions into the hospital was due largely to the increase in the incidence of malaria and influenza, the former being responsible for 37 cases and the latter for 42 cases, and partly to repeated re-admissions.

Malaria still plays an important rôle in the causation of most of the sickness. It has been repeatedly brought under notice in the previous reports of this hospital that the incidence of this disease is progressively high. The same remark is still applicable. Every practicable step has been taken by us from time to time to combat the growing menace of malaria-carrying mosquitoes, but owing to the vastness of the breeding grounds scattered all over the area of Kanke, we have met with little success. Although it is impossible totally to eradicate

this pest, it is within the range of possibility to deal effectively with the mosquito problem, if concerted action were taken by the two mental hospitals (European and Indian), the Agricultural Farm and other Departments stationed at Kanke. Nothing short of this will be of any avail. Accordingly, I addressed the Director of Public Health of this Province in December 1929 on this subject, as a result of which his Assistant in charge of the Chota Nagpur Circle has carried out an investigation as to the extent of mosquito breeding in the area of the European and the Indian Mental Hospitals, the Agricultural Farm, and other places at Kanke, and compiled a report embodying the results of his investigations and indicated therein on what lines a campaign against the mosquito nuisance should be carried out. He suggested, among other things, that the paddy cultivation in the Kanke area might have to be stopped, as the paddy fields are favourite breeding places of malaria-carrying mosquitoes, and emphasised the necessity of appointing a common supervisor or sanitary inspector in charge of the special programme of work suggested by him. The matter is now under consideration of Government.

Health of patients (Physical).—In spite of the striking incidence of sickness, the general health of patients has been good throughout the year under report, and apart from the outbreak of influenza which did not develop to the intensity of an epidemic, there has been no other illness of an epidemic character.

Parole.—It has been more and more realized how valuable the policy of giving parole to patients is an aid to their recovery. As far as possible, all patients of this hospital who are not dangerous to themselves or others, were allowed local and Ranchi paroles. This was also granted to a large number of chronic and incurable cases some of whom were demented considerably, and it was found that they derived a great benefit as a result of receiving this privilege. I am glad to record that in spite of the greater latitude of freedom allowed to them there were no untoward occurrences.

Forms of mental disorder in patients treated.—The following table shows the principal types of mental disorder treated in the hospital during the year under report and in the previous year:—

Types of mental disorder	1929	1930
Circular insanity	21	21
Confusional insanity	3	7
Delusional insanity	17	19
Dementia præcox	54	55
Imbecility	25	29
Insanity from other causes	39	28
Mania	8	13
Melancholia	5	7
Secondary or terminal dementia	53	62
Senile dementia	5	3

Dental treatment.—In view of the increasing recognition of the general harmful effects of oral sepsis, its treatment is an indispensable measure in procuring restoration of the general health and corresponding improvement in mental condition of patients. In furtherance of this view, much greater attention has been paid to the condition of the teeth of every newly admitted patient as well as of those who are already resident in the hospital. The Visiting Dentist, Dr. M. M. Das, has attended regularly throughout the year. I take this opportunity of expressing again my appreciation of the skill and tact with which he has carried out his duties, sometimes in difficult conditions.

Treatment of mental conditions.—The problem of the treatment of patients has received throughout the year our careful consideration in the light of added experience and we continue to make as much progress as possible in this direction.

The following important modes of treatment call for notice:—

(i) *Occupational therapy.*—There is a growing recognition that suitable employment is a direct curative agent in that it produces contentment, diminishes

Annual Reports

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THE Eastern Bureau of the Health Organisation of the League of Nations was established in order to collect and disseminate information of an epidemiological nature in the Far East more quickly than it could be done through Geneva or through the Office Internationale of Paris. The Bureau is located at Singapore. Information regarding outbreaks and incidence of epidemic disease is sent to the Bureau from Far Eastern countries and is quickly collected and sent by telegram and cable to countries and ports all over the Far East and to several ports and countries outside.

The Bureau also compiles an interesting and useful weekly fasciculus of the incidence of epidemic disease in the Far Eastern area. It also publishes an annual report. Dr. Gautier who has acted as Director of the Bureau since its inception has returned to Geneva and his place has been taken by Dr. Park late of the Australian Quarantine Service. The part played by Indian ports in the dissemination of disease in the Far East is well brought out in the report. Calcutta was the port in which cholera infection was contracted in the case of seven vessels out of 19 infected. Calcutta and Shanghai were the two ports from which smallpox infection was exported to the greatest extent.

Of the two vessels found infected with plague one would seem to have been infected at Rangoon. Bombay, Colombo, Rangoon and Bassin remained plague-infected more or less continuously throughout the year. An interesting feature of the report is the evidence of the increased part that the Republic of China is now prepared to play internationally in health matters. Dr. Wu Lien-Teh, already well known for his work on Manchurian plague, is the head of the new National Quarantine Service of China which is dealing particularly with cholera infection and dissemination. A distressing account is given of the floods in China in 1931, relieved by the descriptions of the assistance given by the organisations of various neighbouring and outside countries.

The Bureau has conducted research and liaison work in plague and cholera. The work of Asheshov and Morison on cholera bacteriophage is reviewed and its possible implications pointed out.

The Bureau is destined and fitted to play an increasingly interesting and useful part in the prevention and control of infectious disease in the Far East.

REPORT OF THE EUROPEAN MENTAL HOSPITAL, RANCHI, FOR THE YEAR 1930. BY LIEUT.-COL. O. A. R. BERKELEY-HILL, M.A., D.M., I.M.S. RANCHI: SUPERINTENDENT, GOVERNMENT PRINTING, BIHAR AND ORISSA

THIS annual report is always a most interesting one. The following abstracts from it will serve to summarize it:—

Accommodation.—The accommodation of the hospital during the year under report remained the same as in the previous year, i.e., for 106 males and 100 females or a total of 206 of both sexes.

Summary of notable changes.—There have been very few changes or innovations to record during the past year. I would like to record the acquisition of portraits of the famous men after whom our wards have been named. First we have to thank Dr. Henry Yellowlees, O.B.E., M.D., of the Retreat, York, for a present of a fine portrait of the humane William Tuke, the founder of that institution. Then we have to thank Dr. Lange of the Psychiatric Institute at Munich, for presenting us with a portrait of the late Professor Emil Krapelin,

to be placed in the ward named after this great German alienist. Then our thanks are due to Dr. Daniel, Medical Superintendent of Hanwell Mental Hospital, for presenting us with a photograph of the portrait of Dr. John Conolly, the first English alienist who tried to abolish the habitual cruelty with which the treatment of the insane was notorious up to the end of the 18th century. The photograph was enlarged very successfully so that patients, staff and visitors to the hospital can now gaze upon the handsome face and figure of that pioneer in English psychotherapy. I have also to thank my friend, Dr. Edward Mapother, Medical Superintendent of Maudsley Hospital, for his kindness in permitting me to have a reproduction made of the portrait of Dr. Henry Maudsley that hangs in the hall of the hospital he founded and endowed in London. Portraits of William Cullen and Giovanni Battista Morgagni have also been obtained and they now decorate a wall in the ward named respectively after the great Scottish and Italian reformers of psychotherapy. So far we have failed to obtain portraits of Philippe Pinel and Juan Gilaberto Joffre. For the hospital not yet to possess a portrait of Pinel, the greatest of all the opponents of cruelty to the insane, is very much to be deplored, for Philippe Pinel was the first to adopt, in face of much opposition, an attitude of kindness and sympathy in dealing with the mentally disordered. Further, and this is a point that should never be forgotten in the Rar. Mental Hospital, the first patient in the hospital in Paris, whom he selected for more humane treatment, was an Englishman, a sea captain, who had lived in fetters for no less than forty years. It is pleasant to think that this fierce and powerful madman repaid the wisdom and sympathy of Pinel by henceforth constituting himself the protector of the lion-hearted little doctor from any possible risk of assault that he might have run through suddenly liberating patients from the chains which, combined with many other forms of cruelty, had rendered them both violent and dangerous to the staff of the hospital whom they naturally regarded as their persecutors.

The maximum number of patients resident in the hospital on any one night was 213 (106 males and 107 females) against 206 (106 males and 100 females) in the preceding year.

The number of patients resident in the hospital at the beginning of the year under report was 101 males and 103 females or a total of 204 of both sexes as compared with 193 in the previous year.

The admissions (including re-admissions) during the year under report were 78 (37 males and 41 females) as compared with 62 (35 males and 27 females) in the previous year.

The total population of the hospital for the year under review was 282 (138 males and 144 females) against 255 (125 males and 130 females) in the previous year.

The daily average number resident in the hospital during the year under report was 200.61 (99.90 males and 100.71 females) against 199.51 (97.45 males and 102.06 females) in the preceding year.

Percentage of cases 'cured' and 'improved' to daily average strength.—The annexed table shows the ratio per cent. of cases 'cured' and 'improved' to daily average number resident in the hospital during the year under review as compared with the preceding year:—

Cases		1930	1929
Daily average number resident in the hospital	..	200.61	199.51
Ratio per cent. of cases—			
(a) Cured	..	9.91	5.95
(b) Improved	..	22.43	8.57
TOTAL	..	32.34	14.52

It is satisfactory to note that the number of patients discharged as 'cured', shown in the above table, is considerably higher than that recorded in the previous

the former, a good deal of the defect was possibly attributable to the isolation of Kanke, want of reasonable amenities for recreation and the formation of social cliques. The standard of nursing suffered primarily from the novelty of the work and from the utter ignorance of mental diseases and their treatment on the part of the nurses who elected to work here, a defect due to their training in which no attention is paid to the nursing of mental patients. Now with the increase in understanding of the aetiology of mental disorders as well as of the methods of treating them, the standard of nursing is as high as any one could expect in a country like India.

The more I see of the Anglo-Indian women in the capacity of hospital nurses, the more impressed I am by their talent for this eminently womanly profession.

ANNUAL REPORT OF THE MEDICAL OFFICER OF HEALTH, DELHI, FOR THE YEAR 1931. BY K. S. SETHNA, B.Sc., B.Hy., D.P.H. (LOND.), D.T.M. & H. (CAMB.)

DR. SETHNA'S annual reports are characterised by a refreshing candour and straightforwardness. Conditions are described without any attempt to conceal unpleasant facts; nor is the reader in any doubt as to the opinion of the Health Officer in respect of causation or remedy.

The first outstanding fact in the report is the extraordinary increase in the population of Delhi city in the last decade. Since 1921, the population of Delhi city has increased from 246,987 to 347,592, an increase of over 40 per cent. The reasons given are the centralization of the Government of India in New Delhi and the development of railway work. The increase is therefore probably due in large measure to immigration and is not of a permanently increasing nature. The immediate effect however is likely to be embarrassing to the health of the city. Old Delhi is hemmed in on all sides except the west, and expansion in this direction has been unaccompanied by the ordinary municipal amenities; e.g., the supply of filtered water has not yet been extended to this area. The problem of overcrowding is therefore immediate and pressing, and a committee representative of the municipality has given certain recommendations for expansion of the city which ought to receive very careful consideration by Government. The main avenues for expansion are on and over certain government-owned land, of which the greater part is no longer required for Government purposes, now that the centre of gravity of official Delhi has shifted from the Notified Area to New Delhi. Though one may not necessarily predict a similar expansion of population in the coming decade as in the past, still the problem is immediate, and though the dire effects of the overcrowding do not appear to have been reflected in the 1931 returns to the extent that might have been expected, the problem is a very urgent one and demands the most careful and urgent attention by all concerned. Conditions of overcrowding are most likely to be productive of heavy incidence and mortality from phthisis and this is borne out by the returns for this disease. In 1931, on verification, 1,194 deaths are reported from phthisis giving a death rate of over 3 per 1,000—a very high figure touched only by some other northern Indian towns. The problem of housing in tropical cities is everywhere urgent and difficult.

The birth and death rate for 1931 were 43.4 and 27 respectively—both substantial reductions over 1930 (due almost wholly however to the calculations being made on the new 1931 census). The infantile mortality was 201.2 compared with 198.7 in 1930 and 258.6 in 1929.

The continued absence of plague from Delhi is no doubt due in some measure to the vigorous rat killing campaign continued yearly. In 1931, over 250,000 rats were killed. *X. astia* is the predominant rat flea.

Typhoid fever accounted for 412 deaths—a very high figure. The causes are no doubt the elementary form of conservancy, flies, carriers, and an insufficient and

at times unsatisfactory water supply. Dr. Sethna would hold that the last named is the most potent cause, due to contamination of old and leaky pipes from gross sub-soil pollution. Though supported by medical opinion, this conclusion seems to be disputed by certain lay members of the Committee, and little seems to have been done in the way of remedy. We were under the impression that with the installation of a water carriage system for New Delhi, advantage would be taken to combine old Delhi in the scheme. This seems not to have been the case and the dumping of nightsoil on the outskirts of the city seems to continue with all its attendant dangers and the nuisance of fly breeding still goes on, though the health authorities do their very best.

As regards malaria only 12 deaths were reported but verification by the health staff showed that no fewer than 442 deaths were attributable to malaria. The problem of malaria in and around Delhi has been investigated and reported on at various times. The usual routine measures have been taken but municipal powers seem insufficient to deal with wells.

Maternity and child welfare work is on a good footing; 9 centres exist in the town with a model centre at Bara Hindu Rao attached to the Lady Reading Health School.

The problems of Delhi are thus seen to be mainly of the elementary environmental nature, viz, excretal disposal, water supply and housing. There is no excuse in a modern Indian city for continued neglect of the first two, though housing is a much more difficult matter. Dr. Sethna's report indicates clearly the problems and ways of advance, and we trust that future annual reports will be able to report substantial progress. Dr. Sethna and his staff are to be congratulated on an excellent record of work and energy and on a clearly presented report.

Correspondence

'MILK INJECTIONS IN SPLENIC ENLARGEMENTS DUE TO MALARIA'

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—The conclusions drawn by the author of the above article in the September 1932 issue of your journal seemed to be so very attractive, that it was decided to give this method an immediate trial in our hospital. Accordingly two groups of patients were selected, one of recent cases and the other one of chronic with typical 'ague-cake' spleens. In the recent cases the action of the injections in reducing the size of the spleens seemed to be very doubtful inasmuch as this action is obtained even by the ordinary routine line of treatment of administration of quinine and rubbing of red ointment over the splenic area which of course was kept up in these patients in addition to the milk injections. But in the old and chronic cases the milk injections have absolutely no effect whatsoever and the very bright picture drawn by the author of the article seemed to be very disappointing in our cases.

In short, acute cases of enlarged spleens due to malaria respond quite well to the daily routine treatment of quinine and red ointment. Chronic cases of enlarged spleens due to malaria, in whom milk injections were given according to the author's method and suggestion had not the slightest effect in reducing the spleens, though I venture to say, these spleens eventually become small under the prolonged usual treatment. It is quite possible that the author coming new to a new district came across all acute cases of malarial fever with enlarged spleens, and on giving the milk injections must have been charmed with the result; but those spleens would have disappeared under the usual treatment.

as 1:500 can be employed without damage to the tissues. In non-suppurating wounds the wound may be cleansed with the 1:1,000 solution, the cavity then packed with gauze soaked in the same solution; in suppurating wounds free drainage must first be established, the wound swabbed out once or twice daily with swabs soaked in the same solution, and packed with gauze soaked in it.

In gonorrhœa as a lavage a 1:1,000 to 1:5,000 solution is employed and should be made up in normal saline, being injected twice daily; oral treatment with $\frac{1}{2}$ gr. tablets is also recommended. In local septic conditions the drug may be used as a local application in 0.1 to 1 per cent. aqueous or alcoholic solution. As a poultice 0.6 gm. of 'Acriflavine, B. D.' should be mixed with 4 tablespoonfuls of rice starch, one pint of boiling water added, and the whole boiled until the mixture thickens. Intravenous injection of a freshly prepared 0.5 per cent. solution in a dosage of 1 c.cm. per 10 lbs. of body weight has been reported on favourably in Malta fever, typhoid, meningococcal septicæmia, and also in uterine infections. In pulmonary tuberculosis the hypodermic use of 5 minims doses of a 1:1,000 solution—3 doses in 48 hours—has been recommended. In midwifery a 1:500 solution in glycerine is a valuable and non-irritant lotion, whilst in dentistry 1 to 5 per cent. solutions may be employed for use as a mouth wash in the treatment of pyorrhœa, putrid root cavities, and other cases of oral sepsis.

The drug is put up in powder form, in pessaries, in 1:100 and 1:1,000 solution, and in tablets. The brochure mentioned will be of interest to medical men in general.

LONDON MEDICAL EXHIBITION, NEW HALL, ROYAL HORTICULTURAL SOCIETY, WEST- MINSTER, 17TH TO 21ST OCTOBER, 1932

Notes on the Burroughs Wellcome and Co. Exhibit

The distinctive exhibit of Burroughs Wellcome and Co. demonstrated the attainments in purity and therapeutic efficiency of their products.

Acidosis.—Medical men could test for themselves the palatability of 'Tabloid' Alkaline Compound, Effervescent, a water-dispenser to provide a continuous supply of water having been installed. On solution in water this product provides an effervescent antacid draught, useful as an alkaline diuretic or as a systemic alkaliniser to restore the acid-base equilibrium in acidosis.

Cardiac conditions.—For digitalisation in cardiac conditions 'Diginutin'—a stable solution of the total glucosides of digitalis leaf—may be administered with confidence that the therapeutic effect of digitalis will be attained. For use by ambulatory patients 'Tabloid' 'Diginutin' will be found convenient.

Obstetrics and gynaecology.—'Ernutin' is a clear solution which contains ergotoxine, in definite amount and in a state of chemical purity. 'Ernutin' (oral) contains 0.033 per cent. ergotoxine ethanesulphonate. 'Hypoloid' 'Ernutin' for use by injection contains 0.1 per cent. of ergotoxine ethanesulphonate. Ergotoxine Ethanesulphonate originated and introduced by Burroughs Wellcome and Co. in 1925 is now official. 'Tabloid' Hypodermic Ergotoxine Ethanesulphonate is available.

Radiography.—For use in the radiographic examination of the gall-bladder 'Stipolac' Tetraiodophenolphthalein is supplied in two tubes containing 'Stipolac' Sodium Tetraiodophenolphthalein (Iodophthalein, B. P.) and 'Stipolac' Acid Mixture.

Serological products.—A representative selection of 'Wellcome' Serological products prepared by The Wellcome Physiological Research Laboratories, Beckenham, Kent, England, and distributed by Burroughs Wellcome and Co., formed a section of the exhibit. 'Wellcome' concentrated Gas-Gangrene Antitoxin (*Perfringens*)—Globulins (*B. welchii* = *B. perfringens*) is used for the treatment and prophylaxis of the toxæmia of acute

intestinal obstruction; in certain cases of puerperal septicæmia following abortion; and as a prophylactic against gas-gangrene in grossly infected wounds such as occur in road accidents.

Vitamines.—'Kepler' Cod-liver Oil with malt extract presents vitamins A, B and D in their natural association and is a valuable extra-dietetic agent, especially in childhood and convalescence. A supplementary source of vitamin D is 'Tabloid' Irradiated Ergosterol, while 'Tabloid' Carotene exhibits the characteristic properties of vitamin A.

Medicine chests and cases.—A display of 'tabloid' medicine chests and cases was flanked by photographs of 'tabloid' medical equipment supplied to historic expeditions. A medicine chest carried by Sir H. M. Stanley in the Emin Pasha Relief Expedition in 1887 and rediscovered recently in the Government Medical Stores, Nairobi, Kenya, has been presented to the firm by the Government of Kenya.

The photoscopes.—By means of the photoscopes the characteristic appearance in bold relief of a number of pathological conditions could be viewed. These included leprosy, yaws, syphilis, oriental sore, kala-azar, goitre, cretinism, scurvy, lupus, rickets and acromegaly. Numerous charts and diagrams indicated the trend and attainments of medical science.

MELLIN'S FOOD

The proprietors of this well-known food are issuing a very attractive calendar.

This may be obtained by application to Messrs. Mackenzie Lyall and Co., 5, Mission Row, Calcutta.

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Original Articles

A CASE OF 'ABNORMAL BLOOD GROUP' IN WHICH TRANSFUSION WAS PERFORMED

By R. B. LLOYD, M.A., M.B., B.Chir. (Cantab.)

LIEUTENANT-COLONEL, I.M.S.

Imperial Serologist

and

S. N. CHANDRA, M.B.

Assistant Serologist

(Results expressed in the international nomenclature)

MRS. F. J., an Armenian aged 25, was admitted to the Presidency General Hospital, Calcutta, suffering from anæmia and mammary abscess subsequent to childbirth. The breast was opened and drained, about half a pint of pus being evacuated. Except for an attack of kala-azar six years ago her medical history is unimportant. Her obstetric history is that her first and second children died at the age of one month from 'pneumonia', the third child is alive and apparently healthy, and her fourth pregnancy terminated in the birth of a dead child, three weeks before the present admission to hospital. She has never had a blood transfusion.

On admission she was intensely anæmic and up to the present date has suffered from fever of the continued type. The Widal reaction was negative. The Wassermann reaction was positive, which is interesting in view of the obstetric history. There was some enlargement of the liver and slight enlargement of the spleen. The formalin reaction of the serum for kala-azar was doubtfully positive. It is not possible to determine whether these latter findings are due to the previous attack of kala-azar or to the present attack of syphilis or to both causes. There was no enlargement of lymphatic glands. Blood examination showed the following:—

Red cell count	640,000 per c.mm.
White cell count	5,000
Hæmoglobin	10 per cent.

Differential white cell count:—

Polymorphonuclears	64 per cent.
Lymphocytes	32
Eosinophils	2
Basophils	1
Large mononuclears	1

No abnormal cells were seen.

It will be observed that the anæmia is profound, and that there is no evidence of a polymorphonuclear leucocytosis in response to the septic infection terminating in the large abscess from which *Staphylococcus aureus* was isolated.

As it was desired to perform a blood transfusion, specimens of citrated cells and of whole blood were sent to us as usual for blood grouping tests and the selection of a suitable donor.

Her cells tested for iso-agglutination against sera of known groups yielded the following reactions:—

With group O serum	+
With group A serum	+
With group B serum	+

Therefore as judged from her cells her blood group is AB. Her serum tested for iso-agglutination against cells of known groups yielded the following reactions:—

With group O cells	—
With group A cells	+
With group B cells	—

These serum reactions are abnormal in a blood whose cells are of group AB. Since abnormal types are classified according to the agglutinogens present, the provisional conclusion is that this blood is of group AB with an additional abnormal factor present in the shape of an anti-A agglutinin. As we shall see later, evidence was obtained of the presence of an anti-B agglutinin also.

The following experiments were carried out to determine the nature of the abnormality. For these tests the cells of the patient and those of all persons used for control tests were washed three times, each washing occupying 15 minutes. Using washed cells the above grouping tests were repeated with results identical with those shown above, which were obtained with unwashed cells.

Tests of the patient's cells

1. The cells of the patient were again tested against a fully controlled group O serum. The agglutination was positive. The group of the patient being assumed to be AB, this experiment must yield a positive result.

2. The cells of the patient were tested against six sera of group A, yielding a positive agglutination in each case. This is also the correct result for cells of group AB.

3. Similarly, the cells of the patient were tested against six sera of group B, yielding positive agglutination in each case. This is also normal for cells from a blood of group AB.

Tests of the patient's serum

1. The patient's serum was now tested against cells taken from two fully controlled bloods of group AB. In both cases a positive agglutination was obtained. In one case the reaction was strong, while in the other it was weak. This result is highly abnormal, since the patient's serum agglutinated cells of her own group. The abnormality clearly lies in the patient's serum.

2. The patient's serum was also tested against six sets of group A cells, all fully controlled, yielding a positive agglutination in every instance. This result is also abnormal, since the anti-A agglutinin should not be present in serum from a blood of group AB.

3. The patient's serum was also tested against five sets of group B cells, all fully controlled. This experiment yielded two positive agglutinations, two negative and one positive (weak). This result, which is also abnormal, shows that anti-B agglutinin is also present, though apparently in low titre, since out of five tests two were negative and one positive (weak), and in the original grouping experiment at the head of this paper no evidence of the presence of anti-B agglutinin was obtained. It is well known that the titre of the anti-B agglutinin is often lower than that of the anti-A agglutinin, and the weak positive result obtained in one of the tests detailed in experiment No. 1 above on the patient's serum is probably partly attributable to the low titre of the anti-B agglutinin.

4. The patient's serum was tested for agglutination against her own washed cells. The result was negative. There is thus at laboratory temperature no evidence of auto-agglutination.

5. The patient's serum was tested for agglutination against her own washed cells in the refrigerator. The result was strongly positive, showing that auto-agglutination is present. On placing the preparation in an incubator at 37°C, the agglutination had completely disappeared in five minutes. The reaction is thus reversible.

Absorption tests

The following absorption tests were carried out:—

1. The patient's serum was absorbed overnight in the incubator at 37°C with group A cells. The absorbed serum was then tested for agglutinating power and gave the following results:—

With group AB cells +
With group A cells —
With group B cells +

The absorption has thus removed the anti-A agglutinin.

2. Similarly, the patient's serum was absorbed with cells from one of the group B bloods which yielded a positive agglutination in test No. 3 above with the patient's serum. After absorption, this serum was tested for agglutinating power and gave the following results:—

With group AB cells +
With group A cells +
With group B cells —

This experiment shows that the anti-B agglutinin has been removed by the absorption. It follows that both the anti-A and anti-B agglutinins were present in the unabsorbed serum.

3. A group O serum of known normal reactions was now absorbed with the patient's cells, and the absorbed serum was tested against two sets of group A cells and two sets of

group B cells. In all four tests the agglutination was negative. Since group O serum contains both the anti-A and the anti-B agglutinins which are completely removed by this absorption, this experiment demonstrates the existence of 'A' and 'B' agglutinogens in the patient's cells, thus confirming the correctness of the earlier assumption that the 'normal' group of the patient is AB.

This patient's blood thus contains both 'A' and 'B' agglutinogens and a and b agglutinins, a combination which, if effective *in vivo* at body temperature, would be incompatible with life.

Tests to investigate the connexion, if any, between the abnormal blood group and the auto-agglutination

Fortunately sufficient material was available to permit of these crucial tests being carried out in a test tube, and it will be seen later how this circumstance enabled us to determine the nature of the abnormality.

The patient's washed cells were placed with her own serum in the refrigerator overnight (using an excess of cells). As before, a strongly positive agglutination was obtained. After the absorption, the supernatant serum was withdrawn by capillary pipette while the whole preparation was still in the refrigerator. This absorbed serum was now tested against cells of groups A and B yielding negative reactions in both cases.

This experiment demonstrates that after removal of the auto-agglutinins by cold fixation the serum has reverted to normal as regards iso-agglutinins, since in group AB the serum has no agglutinating power. Sufficient material was available to permit of the repetition of this test on a subsequent day, and the results were identical.

We have thus been able by absorption in the cold to dissect, as it were, the agglutination phenomena produced by this serum of 'abnormal group' into two components which separately produce:—

(i) Entirely normal reactions corresponding to group AB (absence of iso-agglutinins).

(ii) Auto-agglutination, which, in so far as the patient's own cells are concerned, exhibits the usual properties of occurring only in the cold and being reversible on warming, yet occurs at laboratory temperature with cells of groups A and B and even with cells of other group AB persons, *i.e.*, the same group as the patient.

We again performed this experiment of placing the patient's cells and her serum in the refrigerator overnight, but instead of pipetting off the serum in the cold, we varied the technique by removing the preparation from the refrigerator and centrifuging it at laboratory temperature and then pipetting off the serum for test. The time occupied by this operation was two minutes. The absorbed serum obtained under

these conditions yielded the following reactions:—

With group A cells +
With group B cells ±

It will be seen that by this variation in technique an entirely different result is obtained. This last experiment demonstrates the surprising rapidity with which the auto-agglutinins again become free in the serum when the preparation is even slightly warmed, reproducing the apparent 'group abnormality'.

We are thus dealing with a blood whose cells give normal reactions for group AB, and whose serum also gives normal agglutination reactions—these are of course *nil* in the case of group AB—provided the auto-agglutinins present are rigidly excluded by decantation of the serum under strict refrigerator conditions after absorption with the patient's own cells.

We now desire to refer to a previous publication by us on a very similar case (Lloyd and Chandra, 1930). Both the patients were women, both were suffering from anaemia, in both the basic group was AB, and in both cases auto-agglutinins were demonstrated. In our former case the cold-box absorption tests to remove the auto-agglutinins could only, owing to shortage of material, be carried out once on a slide. In view of the reactions of the present case which demonstrate the amazing rapidity with which auto-agglutinins fixed by the patient's own cells in the cold again become free on the slightest warming, we have to admit the possibility that the technique described in our former paper for removal of the auto-agglutinin may not have been entirely adequate. This involves the possibility that the post-absorption agglutinations in our first case were in reality due to released auto-agglutinin, and not, as we thought at the time, to an independent abnormality. If this be so, the two cases fall into the same class, both exhibiting auto-agglutination at laboratory temperatures against cells of groups A and B, and even in the latter case against cells of group AB, though against the patient's own cells the agglutination only occurs in the cold, being reversible on warming.

It is of importance to determine whether auto-agglutinins are more prone to appear in the group which has no iso-agglutinins than in any other, or whether it is only a coincidence that in our seven years experience of blood grouping, during which over a thousand such tests have been carried out, only two instances of auto-agglutination have been found, which in both cases were in group AB blood.

It is natural to suppose that, when this patient was in a condition of health, she had a normal group of the AB type, and that, connected in some way with the onset of the grave anaemia, the auto-agglutination effect developed. This being added on, as it were, to the normal reactions of the blood suggests the existence of an abnormal blood group. If this patient

survives, as seems possible, we hope to be able to examine her blood again some months hence in order to see the effect of recovery on the auto-agglutinins.

As regards the possibility of blood transfusion, we first reported to the physician that in view of the abnormal reactions of the patient's blood we could not guarantee any donor as safe, and recommended that blood transfusion be not given. The physician, however, considered that without a blood transfusion the prognosis was so grave that the risk of untoward results from a transfusion must be faced. We were asked to reconsider the question from this point of view, and we agreed, on the understanding that the laboratory incurred no responsibility, to provide a donor. Even though the patient's serum does not agglutinate her own group AB cells *in vivo*, we must, in selecting a donor, depend upon the reactions of the blood examined *in vitro*. As her serum agglutinated group AB cells *in vitro*, transfusion with group AB blood was clearly inadmissible. She was therefore in the curious position of being debarred from receiving blood of her own group. As both anti-A and anti-B agglutinins were present in the serum it was clear that the only chance for this patient was a donor entirely devoid of agglutinogens, *i.e.*, one of group O. In view of the possibility of further abnormal reactions, we carefully tested the serum of the patient against the cells of the selected group O donor, the result being negative as it should be. We accordingly advised the physician that theoretically there was no more risk in transfusing this patient with a universal donor than was attributable to her extreme anaemia—the unavoidable incompatibility between the donor's serum and the recipient's cells being assumed to be maximal in cases where the recipient's red count is very low—but that in practice we could not tell what might happen. It was also advised that the transfusion be limited to 150 c.cm. of blood given very slowly.

Transfusion was carried out with complete success, the only reaction being a very slight rigor. We suggested that special watch should be kept for haemoglobinuria; however this was entirely absent. The presence of auto-agglutinins was thus no bar to a successful transfusion, though we should not in the circumstances have been prepared to take the risk of neglecting the auto-agglutination phenomena by recommending the transfusion of such a case with blood of the same group. This comment would not apply to group O recipients. In all cases where abnormal agglutinins are present the donors selected should be of group O and very careful cross testing is required.

Conclusions

1. In a case of grave anaemia the blood was found to be of group AB type with normal cell reactions and abnormal serum reactions,

2. Auto-agglutination in the cold was also present.

3. Removal of the auto-agglutinins by incubation with the patient's own cells at refrigerator temperatures removed the abnormality from the serum.

4. The apparent abnormality of the blood group is thus due to the addition of the auto-agglutinin effect to the normal reactions of the serum.

5. The presence of auto-agglutinins is not necessarily any bar to a successful blood transfusion, though only group O donors are admissible in such cases, and careful cross testing is essential.

6. As this patient has a history of kala-azar and is at present suffering from syphilis, this case is no exception to the usual experience that auto-agglutinins only appear in human serum during grave disturbances of health.

Acknowledgments

We are greatly indebted to Lieut.-Colonel A. H. Proctor, D.S.O., I.M.S., Surgeon Superintendent, Presidency General Hospital, Calcutta, for the opportunity of examining this blood, and to Dr. S. J. G. Nairn, Resident Surgeon of the hospital, for the use of his clinical notes.

REFERENCE

Lloyd, R. B., and Chandra, S. N. (1930). A case of highly abnormal blood group associated with auto-agglutination in the cold. *Indian Med. Gaz.*, LXV, 1.

DIET AS A POSSIBLE FACTOR IN THE CAUSATION OF STONE IN THE BLADDER IN THE PUNJAB

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THIS note deals with an attempt which was made to find out whether the incidence of stone in the bladder in the three chief communities of the Punjab would throw any light on the relationship between diet and stone formation. The important work of Col. McCarrison and other investigators strongly suggests that diet is a factor of great importance in connection with stone formation.

The data contained in the table were supplied by the civil surgeons of the Punjab; I am much indebted to them and to the former Inspector-General of Civil Hospitals, Col. Mackenzie, C.I.E., I.M.S., for all the trouble they have taken in obtaining the information which was asked for.

It will be seen that the incidence of stone is much lower in Sikhs than in the other two communities, being only half that in Hindus

and less than one-third of that in Muslims. The figures for cataract were obtained partly to serve as controls and partly to find out whether any significant differences existed in the prevalence of cataract among the members of the three communities. The percentage incidence of cataract is almost the same in Muslims and Sikhs, while that for Hindus is somewhat lower. If, however, the large figures for the Mathra Das Dispensary of Moga had been included, there would actually have been a higher incidence in Hindus than in Muslims, so that there is no evidence of any significant difference in the incidence of cataract among the three communities. The figures for Moga had to be excluded partly because Sikhs were not shown separately in the returns, having been grouped among the Hindus and partly because patients go to Moga from all parts of India.

An attempt was made to find out from the civil surgeon whether the diets of the three communities differed in any important respects, but the evidence on this subject does not justify the expression of any clear-cut statement, except on broad general lines. It is generally agreed (a) that on the whole Hindus take more milk, fruits and vegetables than Muslims, (b) that Muslims eat much more meat than Hindus, (c) that the Sikhs have a more varied and more nutritious diet than either of the two other communities and that on the average they drink more milk than do the members of the other communities. According to Col. McCay the average daily diet of adult Sikhs consists of—milk 16 ounces, wheat 24 ounces, butter 2 ounces, dal 3 ounces, vegetables 6 ounces, and meat 4 ounces. This is certainly a much better diet scale than that of the other communities, it contains notably more milk than the diet of the Muslims, more meat and milk than that of the Hindus. With regard to the amount of wheat that is eaten by the people of the three communities it is impossible to make any dogmatic statement.

The figures are of some interest, they suggest that the tendency to stone formation is less among people who eat a well-balanced and nutritious diet containing a large proportion of milk than among those whose diets are unsatisfactory in these respects. It would be unjustifiable to claim that the data demonstrate a definite relationship between special kinds of food and the formation of stone, but at any rate they suggest that valuable information on the subject might be obtained by making a detailed enquiry in the Punjab.

A factor which may be of importance is the Ramzan fast. For a month in each year all strict Musalmans observe a strict fast from sunrise to sunset; the deprivation of water, especially when the fast falls in the hot dry season, must cause a high degree of temporary dehydration and concentration of the urine.

Table showing the incidence of stone in the bladder among the communities of the Punjab during the three years from 1928 to 1930

Name of district	STONE			Percentage of stone to total admissions	Caste			ALL IN-PATIENTS			Total
	Hindus	Muslims	Sikhs		Hindus	Muslims	Sikhs	Hindus	Muslims	Sikhs	
Ambala ..	18	31	..	1.12	143	126	14	1,201	1,152	233	2,586
Amritsar ..	42	170	45	1.59	1,128	3,488	1,784	3,889	6,742	5,443	16,074
Campbellpur ..	1	26	..	1.82	17	140	..	161	1,300	20	1,481
Dera Ghazi Khan ..	33	180	..	1.06	8	142	..	327	1,670	5	2,002
Ferozepore ..	11	74	2	4.33	11	6	..	674	1,110	225	2,009
Gujranwala ..	10	52	8	4.19	1	6	..	532	921	216	1,669
Gujarat ..	8	76	..	4.87	1	22	..	313	1,410	..	1,723
Gurdaspur ..	21	21	2	1.67	86	104	50	932	1,065	632	2,629
Gurgaon ..	28	17	..	2.13	266	145	..	1,496	607	..	2,103
Hissar ..	31	8	..	4.1	4	2	..	764	187	..	951
Hoshiarpur ..	20	35	..	3.32	46	103	1	653	768	233	1,654
Jhelum ..	5	77	..	4.77	11	127	1	236	1,420	62	1,718
Jullundur ..	44	114	22	3.53	232	510	53	1,703	2,702	681	5,086
Kangra ..	11	1.35	14	3	..	679	127	3	809
Karnal ..	24	9	..	2.65	25	34	..	931	314	..	1,245
Lahore ..	96	208	29	2.00	193	490	38	6,028	8,168	2,428	16,624
Ludhiana ..	21	21	8	2.1	12	26	3	765	1,081	642	2,488
Lyallpur ..	22	80	5	4.62	3	4	1	595	1,293	428	2,316
Goira (Dist. Lyallpur)	17	55	19	0.58	1,543	2,531	552	4,979	7,676	2,896	15,551
Maghiana ..	28	101	2	5.68	9	64	..	632	1,636	37	2,305
Mianwali ..	13	81	..	4.28	20	309	..	217	1,959	20	2,196
Montgomery ..	44	77	1	4.87	12	36	1	740	1,400	361	2,501
Multan ..	59	259	1	11.61	9	60	..	879	1,721	65	2,668
Muzaffargarh ..	20	136	..	8.82	9	143	..	408	1,326	34	1,768
Rawalpindi ..	18	68	6	1.70	76	349	13	1,281	3,783	345	5,409
Rohtak ..	42	18	..	4.22	6	6	..	1,050	369	1	1,420
Sargodha ..	20	104	7	3.80	14	19	..	1,021	2,215	208	3,444
Sheikhpura ..	4	8	3	1.02	29	69	8	279	809	369	1,457
Sialkot ..	22	86	6	3.99	95	275	5	780	1,922	153	2,855
Simla ..	22	6	..	0.91	15	5	..	2,061	986	..	3,047
Total ..	755	2,098	166	2.75	4,038	9,344	2,526	36,206	57,842	15,740	109,788
Percentage of cases to total admissions of each community.	2.08	3.62	1.05	..	11.15	16.15	16.05

CYTOLOGICAL STUDIES OF THE BLOOD AND TISSUES IN KALA-AZAR AND ASSOCIATED CONDITIONS

Part IV.

THE LARGE MONONUCLEAR CELLS IN MONKEY MALARIA

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IN a previous paper we recorded the results of a preliminary investigation on the large mononuclear changes in the blood of human beings suffering from malaria (Napier, Krishnan and Lal, 1932). In that paper, on account of the small number of cases studied, we could draw only tentative conclusions regarding the functional rôle of the two types of large mononuclear cells in malarial immunity. While that investigation was in progress Napier and Campbell (1932) found a plasmodium in the blood of a monkey, *Macaca irus* (*Macacus cynomolgus*), which while producing only a chronic type of low-grade infection in members of this species gave rise to a rapidly-progressive and fatal form of infection in monkeys belonging to the species *Macaca mulatta* (*Macacus rhesus*). This gave us an opportunity to investigate in detail the qualitative and quantitative changes in the large mononuclear cells of the blood in monkey malaria, from the very commencement of infection to its termination, and to obtain more conclusive data regarding the function of the large mononuclear cells. Altogether we studied supravital preparations of blood obtained from eighteen infected monkeys at different stages during the progress of infection and of immunity. In this paper we have presented some of our observations; these appear to us to show that histiocytes and monocytes are jointly responsible for the overcoming of the malarial infection, but that they differ from one another in the manner in which they produce their effect.

Source of material

In order to obtain samples of blood from infected monkeys at all possible stages of infection and immunity the following course was adopted. Twelve *M. mulatta* and six *M. irus* monkeys in a healthy state were obtained and before infecting them with the plasmodium the blood of each was examined a few times in order to make sure that all were free from parasites and to obtain a true normal picture of the blood cell elements, particularly of the large mononuclear group. Each animal was then given approximately the same dose of infective material subcutaneously (about 5 drops of heavily-parasitised blood from a *mulatta* monkey, mixed with 10 drops of citrated saline),

and thereafter a daily examination of its peripheral blood was made for the presence of parasites, and for ascertaining the large mononuclear changes.

Out of the 12 *mulatta* monkeys inoculated one proved refractory and 11 developed infections after periods varying from 3 to 12 days; their pre-patent* periods were 3, 3, 4, 5, 5, 5, 5, 6, 8, 9, and 12 days, respectively. Of the 11 infected monkeys, four were given no treatment and their infection was allowed to run its natural course; three of these died within six days of the commencement of the patent* period. The parasite count showed a rapid and progressive rise until it reached nearly a million per cubic millimetre of blood before death. The fourth monkey showed a tendency towards natural cure and survived for a period of 32 days without treatment. During this period the parasite counts showed great fluctuations and on the 25th day no parasite could be found. For the next 7 days all examinations were negative, but on the 32nd day its condition suddenly became worse and its blood again showed a few parasites. Administration of quinine helped it to tide over the crisis and ultimately to get rid of the infection. The remaining 7 monkeys were all given treatment as soon as their general condition became bad or the parasite rate rose to about half a million per cubic millimetre of blood, which number was generally reached within 3 or 4 days of the commencement of the patent period of infection. In this treated group one died suddenly, 51 days after infection and 30 days after completion of treatment that had been continued until all the parasites in its peripheral blood had completely disappeared and the animal had received a total of about 15 grains of quinine. For nearly a month preceding its death its blood had been free from parasites, but after death post-mortem examination of spleen and liver smears showed a fair number of developmental forms of the parasite. In four of the remaining six treated monkeys, quinine has so far had only the effect of preventing fatal issue in the acute type of infection and converting it into a chronic relapsing type. During the past four months these monkeys have had several relapses after latent periods varying in duration from a few days to a few weeks. Only two of the treated monkeys, which had heavy doses of quinine over a long period, have been cured so far. In these not only have we failed to find parasites

* We are using the words *patent* and *pre-patent* at the risk of offending purist readers, because we know no other single words that express so well the ideas we wish to convey; the *pre-patent* period is the period between the inoculation of the virus and the appearance of the parasites in the peripheral blood (in sufficient numbers to be demonstrated by the methods at our disposal), and the *patent* period is the period during which parasites can be found in the peripheral blood. We claim no originality, and we append this explanatory note only because the words are not in common use in this country.

after repeated examination of their peripheral blood, but inoculation of the blood into healthy monkeys has also failed to produce infection.

The one 'refractory' monkey was given two more heavy doses of infective material at fortnightly intervals and eventually it developed malaria five days after the third massive dose of infected material (table IX).

As regards the 6 *irus* monkeys all but one became infected, the pre-patent periods of these five being 6, 7, 7, 11 and 36 days, respectively. These remained untreated for a period of two months and during this period they all showed a relapsing type of low-grade infection with the parasite count at no time reaching a maximum of more than a few thousands. After several relapses two of the monkeys were given quinine; this resulted in the prompt disappearance of the parasites and so far they have not relapsed. Of the three others remaining untreated, one died, probably of some intercurrent disease, post-mortem examinations of spleen and liver smears showing a few parasites, and the remaining two monkeys showed a low-grade relapsing type of infection for nearly 3 months. Examination of these monkeys after the lapse of six months revealed that both of them had successfully got rid of the infection and that they were resistant to re-infection. Three attempts to infect the refractory monkey proved completely futile.

From the above summary it will be evident that the material for the study of the mononuclear changes was obtained from a number of different monkeys during a great variety of phases of infection and immunity.

Technique

Supra-vital preparations of blood as well as fixed films, stained by Giemsa's method, were studied. The technique of supra-vital staining was the same as that described by us in a previous paper (Napier, Krishnan and Chiranjilal, 1932a). Total counts of the leucocytes, and parasites were also obtained. In order to avoid errors due to sampling and the personal factor in the counts, we made at the least two preparations on each occasion and recorded the average of the counts made by two observers, working independently of one another. For the purpose of the differential counts the number of leucocytes counted by each worker in any one slide was never less than 100.

Results

Though in a few instances we were able to follow the blood-cell changes in an individual monkey as the infection passed through its various stages of invasion and culmination, or latency and regression, the gaps which necessarily occurred in such records detract from the value of the picture they present, and we have thought it best to group and give in separate tables the counts obtained at different clinical stages of infection and recovery, irrespective of

the individuals from which the blood was obtained, only showing separately the counts in the two different species of monkey. These counts are shown in tables I to IX.

The following is a brief summary of the findings as shown in each table:—

Table I shows that the total large mononuclear count in normal *mulatta* and *irus* monkeys is about 4 per cent. and is composed chiefly of monocytes. There appears to be no difference in the counts in the normals of the two species with regard to this cell type.

Table II shows that during the pre-patent period of infection there is little or no change in the total large mononuclear count of the *mulatta* monkey, but that there is perhaps a slight tendency for the intermediate forms and the histiocytes to increase at the expense of the monocytes. In *irus* monkey on the other hand there is a definite increase in the total number of large mononuclear cells brought about by an increase of intermediate forms and histiocytes, the monocyte count showing little change.

Table III shows that on the first day of the patent period in the *mulatta* monkey there is a distinct rise in the number of total large mononuclear leucocytes and that this increase is due chiefly to a rise in the number of histiocytes and intermediate forms. The monocytes show a distinct fall. The *irus* monkeys show under similar circumstances a more marked increase in the large mononuclear cells and here the rise is due to increase in all three forms.

Table IV shows that in both species of monkey about the middle of the patent period when parasites are fairly numerous and the animals not too ill, the large mononuclear count is distinctly high and that this increase is brought about by a rise in the number of intermediate forms and histiocytes, the monocyte count showing very little change.

Table V shows that when the *mulatta* monkey is looking very ill as a result of the infection and on account of a failure of its immunity response there occurs a fall in the total large mononuclear count, the fall being attributable chiefly to a decrease of the histiocytes and to a smaller extent of the monocytes.

Table VI shows that a day or two before death in the *mulatta* monkey there is a tremendous drop in the total large mononuclear count and this is brought about by a decrease in all forms, particularly monocytes.

Table VII shows that administration of quinine is followed by an increase of all forms of large mononuclears and specially of histiocytes and intermediate forms. This change is best seen in the *irus* species.

Table VIII shows the similarity between the cytological changes taking place in animals with a tendency for natural cure and those that are recovering as a result of treatment with quinine. Here again the rise in histiocytes and intermediate forms are most marked.

Table IX shows that in resistant monkeys following the inoculation of infective material there generally occurs a prompt and marked mobilisation of the large mononuclear cells in the peripheral circulation.

Table A. A summary of tables I to VIII.

The changes in the percentages of the different large mononuclear cells in the peripheral blood

The changes which occur in the large mononuclear counts during the various phases of the malarial attack can be seen in tables I to VIII, at the end of the paper; they are summarized in table A and shown in graphic form

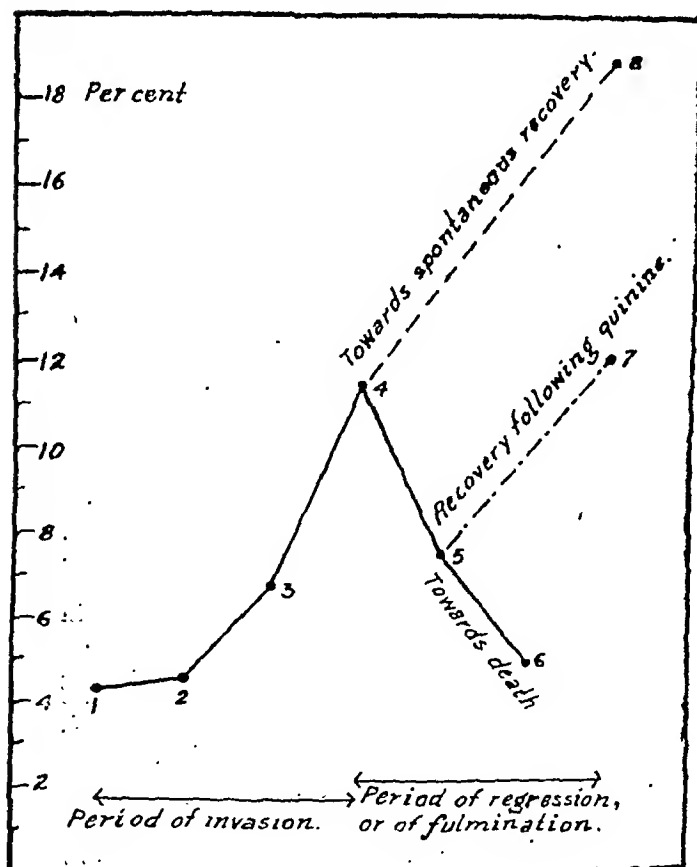
TABLE A

Showing the mean percentage distribution of the different types of large mononuclear cells in the blood of normal monkeys and of monkeys in different stages of a malarial attack; a summary of tables I to VIII

	Table from which means are taken	Stage of infection	Number of observations on which based	Total leucocytes	Total large mononuclears	Monocytes	Intermediates	Histiocytes
<i>M. mulatta</i>	I	Normal	10	15,300	4.4	4.0	0.4	0.0
	II	Pre-patent	9	13,319	4.6	3.1	0.8	0.7
	III	Early patent	9	13,444	6.8	1.8	1.8	3.2
	IV	Mid-patent	16	16,852	11.5	2.7	5.9	3.0
	V	Heavy	16	14,656	7.5	2.4	3.4	1.8
	VI	Overwhelming	8	14,250	5.0	1.3	1.9	1.8
	VII	Quinine	21	16,098	12.1	3.8	4.2	4.1
	VIII	Natural recovery	2	18,250	18.5	5.0	6.8	6.8
<i>M. irus</i>	I	Normal	6	15,688	4.2	4.0	0.2	0.0
	II	Pre-patent	5	17,850	5.9	2.7	2.3	0.9
	III	Early patent	5	16,225	9.4	6.0	2.2	1.2
	IV	Mid-patent	8	17,675	10.0	3.6	3.4	3.0
	VII	Quinine	4	19,000	18.3	7.0	6.0	5.3
	VIII	Natural recovery	11	18,041	14.5	5.6	5.6	3.3

in chart I. In *Macaca mulatta* monkeys the normal appears to be about 4.4 per cent. of

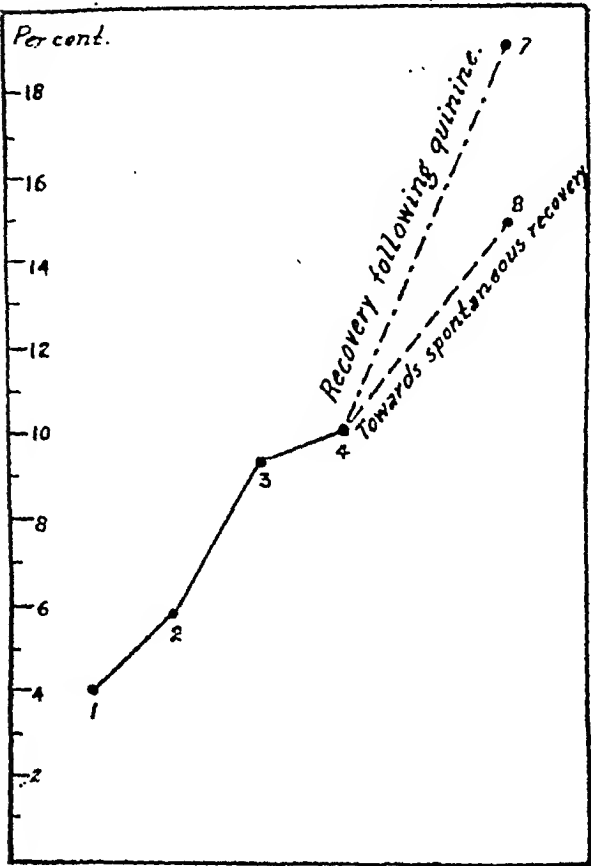
CHART I



the total white cells. In the early patent stage of infection there is a distinct rise in the percentage of large mononuclears and this rise is even more marked later, as the parasite count rises. The fate of the animal now appears to depend on whether the mononuclear count is maintained or not; if there is a further rise the animal recovers and the infection disappears or passes into a latent stage, but if the mononuclear response fails and the count falls the infection gets the upper hand; at this stage if the failure is not too complete quinine administration will often result in a sharp mononuclear rise and will save the animal. In *Macaca irus*, in which species recovery is the rule, the mononuclear rise occurs earlier; the administration of quinine causes a further very marked mononuclear response which is usually followed by complete disappearance of the parasites. If no quinine is given then the infection usually passes into the latent stage and a moderately-high large-mononuclear count will be maintained (chart II).

The behaviour of each of the three types of cell in the mononuclear group is not the same. We will consider the monocytes first; in the pre-patent and early patent stages there is an apparent fall which is almost entirely compensated for by a rise in the number of the intermediate forms. This suggests that some of the monocytes have taken on an increased phagocytic function which qualifies them to be classed as intermediate forms. If we consider the monocytes and intermediate forms together, which whilst considering the question of the monocytic response seems justifiable, as there is little doubt that they have a common origin, we see that in the *M. mulatta* series (chart

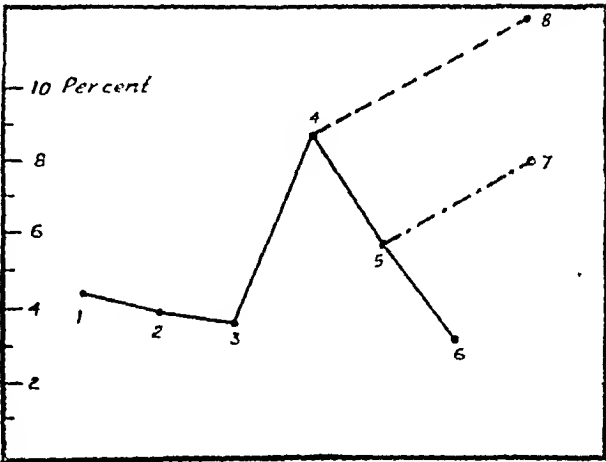
CHART II



The large-mono-nuclear response at various stages of a malarial attack in a *M. irus* monkey. See letter-press to chart I.

III) there is no sign of any rise in the early stages of the infection; there is in fact a slight though insignificant fall. At a later stage of

CHART III



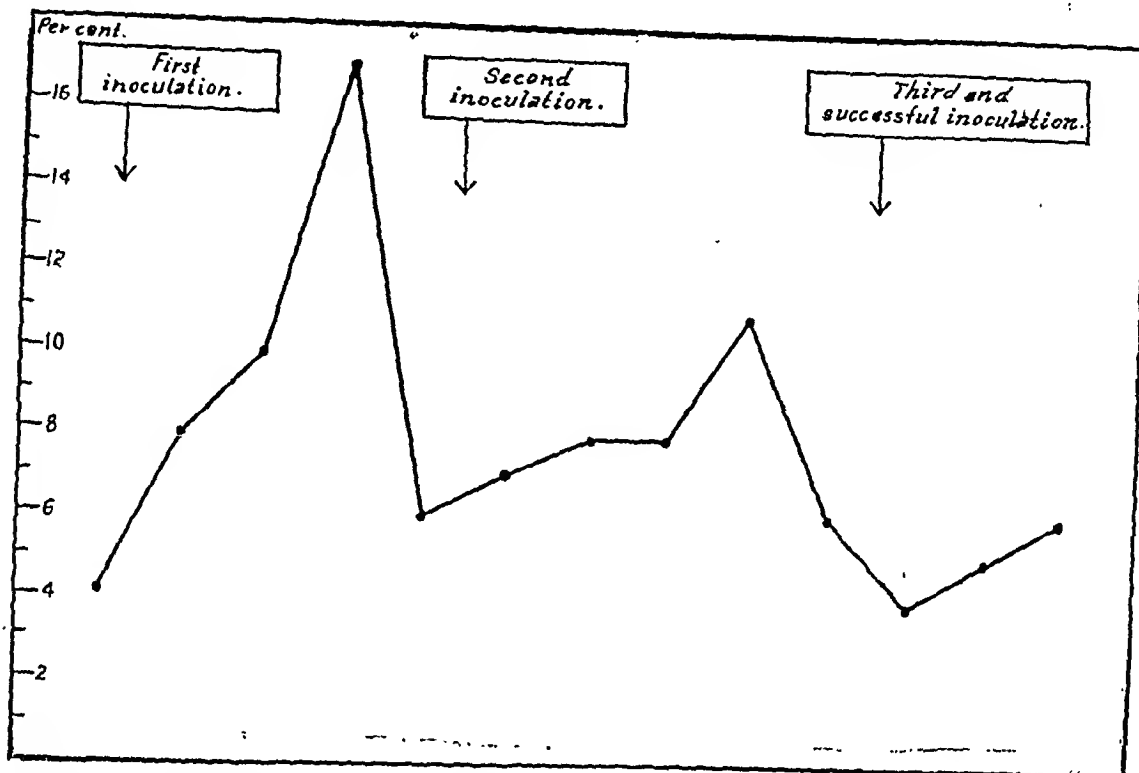
The monoocyte response at various stages of a malarial attack. See letter-press to chart I.

the infection, when possibly a destruction of a certain number of parasites has provided the necessary stimulus, there is a sharp rise; after this the monoocyte curve follows the general large mononuclear curve. In monkeys refractory to infection there is an early monoocyte response to the dose of morbid material, which appears to prevent infection occurring (table IX and chart V).

TABLE IX

Stages at which count was done	M. mulatta					M. irus				
	Total leucocyte count	Total large mono-nuclears	Mono-cytes	Inter-mediates	Histio-cytes	Total leucocyte count	Total large mono-nuclears	Mono-cytes	Inter-mediates	Histio-cytes
Prior to inoculation of infective material.	9,000	4	3	1	0	12,000	5	4	1	0
A few days after inoculation of infective material which caused no infection.	7,500	8	6	2	0	20,000	15	9	5	1
	10,000	10	5	4	1	25,000	15	10	4	1
	12,500	17	9	8	0	19,000	15	8	7	0
						22,500	17	12	4	1
Prior to inoculation of 2nd infective dose.	10,000	6	4	1	1
A few days after inoculation of 2nd infective dose which caused no infection.	9,000	7	4	2	1	19,000	15	7	6	2
	10,000	8	4	3	1					
	8,875	8	5	3	0					
	10,000	11	6	5	0					
Prior to inoculation of 3rd infective dose.	9,000	6	5	1	0
A few days after the 3rd infective dose which resulted in the infection of the <i>M. mulatta</i> .	10,000	4	3	1	0	22,000	17	8	7	2
	7,500	5	2	2	1					
	11,250	6	2	2	2					

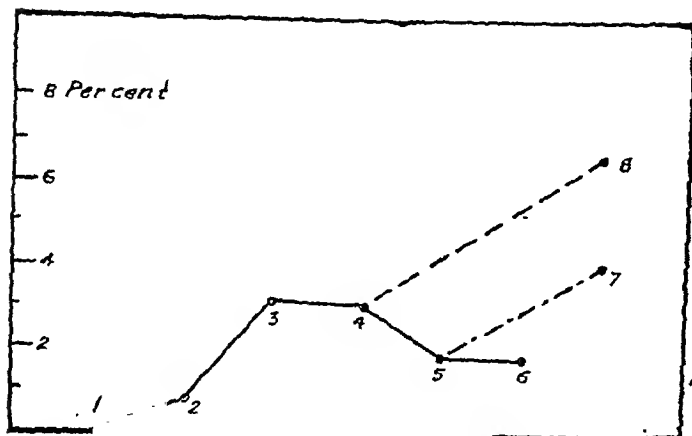
CHART V



The large-mononuclear response to inoculation with morbid material in a *M. mulatta* monkey which at first proved refractory to malarial infection. The ordinates are the large mononuclear percentages of individual differential white counts; the abscissæ are arbitrarily spaced.

On the other hand the histiocytes which are not normally present in the peripheral blood make their first appearance at an early date in the infection, some time before the monocytes start to rise, they then follow the general mononuclear curve (chart IV). However, the sharp

CHART IV



The histiocyte response at various stages of a malarial attack. See letter-press to chart I.

rise (table VIII) which is associated with recovery of the animal is not maintained as in the case of the monocytes and when the infection passes into the latent phase the histiocytes drop to 1 or 2 per cent. (This is not shown in either the tables or the charts.)

Function of the large mononuclear cells

As far as we are aware very little work has been done to determine whether or not the two

types of large mononuclear cell, monocytes and histiocytes, are different in function. During the present investigation therefore in addition to noting the quantitative changes, already recorded above, we took particular pains to study the behaviour of the several types of mononuclear cells in our supra-vital preparations, hoping thereby to ascertain how far their functions, as regards resistance and cure in malaria, can be said to be similar or dissimilar. Our findings and views are discussed below.

Histiocytes

Some of the earlier workers on malaria have suggested that the histiocytes are probably the phagocytes chiefly responsible for the destruction of the malarial parasites (*vide* Napier, Krishnan and Lal, 1932). The results of this investigation show that the histiocytes are undoubtedly the best phagocytes. We have repeatedly seen them in supra-vital preparations containing a variety of objects, such as red cells—infected and uninfected, pigment, platelets and cell debris of various sorts, as well as a large amount of neutral red (*vide* plate). This leaves no doubt whatsoever regarding their phagocytic capacity. When, however, we come to consider whether the histiocytes take up living malarial parasites, and, if so, whether they kill and digest them as well, we must admit that we do not possess sufficient evidence to justify the expression of a definite opinion. We attempted to study the powers of destruction of the histiocytes at

various stages of malarial infection by watching the changes taking place in the ingested parasites within living histiocytes for varying periods of time. We also noticed their method of disposal of the parasites after the administration of quinine and other anti-malarial remedies, and saw that whereas in the early stages of infection the histiocytes contain mostly pigment, or occasionally a red cell, that later, when infection is progressing, they are seen with pigment, parasites and parasite-infected red cells showing undoubted evidence of varying degrees of destruction and digestion, that still later, when the infection is well established and severe, and the animal is losing ground, the histiocytes again contain fewer parasites and more pigment, some of the parasites contained appearing perfectly healthy and showing no evidence of degeneration (*vide* plate, fig. 2), and that finally as the infection is reaching a fatal termination the histiocytes' powers of phagocytosis and destruction, as well as their number (*vide supra*), are found to be at a minimum. Even the amount of neutral red taken up by these cells is sometimes very small at this stage. If, however, either on account of increased natural resistance or of the administration of quinine or other specific drugs, the animal gains the upper hand, then accompanying the sudden and sharp rise in the number of histiocytes (*vide supra*) there is a marked heightening of the phagocytic and destructive powers of the majority of these cells. From these observations we are led to infer that the histiocytes under certain conditions, though not always, are capable of taking up living parasites, and killing and digesting them; biochemical conditions within the host possibly determine whether or not such an action takes place. We have evidence that under certain adverse conditions these cells may not have the power to destroy the parasites but require the help of other factors before their destructive powers can be brought into play. Even so the importance of histiocytes in the cure of malaria is unquestionable. The mere fact that the histiocytes are helpful in the phagocytosis and removal from the circulating blood of a large number of infected red cells to the internal organs for the purpose of effective destruction, is in itself sufficient to give the histiocytes an important place in malarial immunity, for such an action will form an effective check in the schizogony cycle.

It is generally accepted that the histiocyte, whether in the blood or in the tissues, is primarily concerned with the disposal of damaged and degenerated red blood corpuscles. Naturally therefore it will ingest any red cell that is damaged, irrespective of the cause of damage. There is every reason to believe that the entry and development of the malarial parasites within the red cells damages these cells, which are therefore engulfed by the histiocytes. It is possible that the histiocytes take

them up not for the destruction of the parasites that they contain but for the disposal of damaged red cells themselves. The destruction of the parasite when it takes place may thus be purely circumstantial. It is unnecessary to discuss whether it is brought about by the unsuitability of the condition within the cell interior or by an inherent lytic capacity possessed by the cell. Whatever it may be all evidence supports the view that some of the parasites at any rate are destroyed by the histiocytes.

The function of the intermediate forms

In our previous communication we suggested that the intermediate forms possibly originated from monocytes in response to stimuli demanding more phagocytic cells but that with regard to function they should be treated as young and active histiocytes because of their more marked similarity to these than to the monocytes. We still hold this view and consider that as far as function is concerned these cells should be classified with the histiocytes. Although in the intermediate forms one does not find the same variety of ingested material within their cytoplasm as in the histiocytes, under the stress of a suitable stimulus the former appear to be as efficient phagocytes as the latter though perhaps more selective in their choice. We think they are chiefly concerned with the phagocytosis of free or living parasites, for, although they have been seen containing infected red cells, they do not show them quite as frequently as the histiocytes. They are more often found with pigment and debris, and this we think is not because they take up only pigment but rather because they are capable of digesting the engulfed parasites with greater rapidity than are the histiocytes. We have on a few occasions actually seen these cells taking up into their cytoplasm what appeared to us to be malarial parasites. The process of lysis was very rapid and it was over before we could make a *camera-lucida* drawing of what we saw. All we could see in these cells after the lapse of some seconds was particles of pigment (*vide* plate, fig. 4). It appeared as if the cell on ingesting the parasite segregated it at the *hof* of the nucleus where there seemed to be a distinct round vacuole-like area. Here everything that was engulfed was isolated and lysed, and the black pigment or debris resulting from it sent out to the periphery of the cell. On one occasion we saw a cell actively progressing towards a collection of infected red cells in a zig-zag way (*vide* plate, fig. 10); we saw within its cytoplasm pigment and certain other bodies resembling fragments of parasites; as it reached the collection of infected red cells it became sluggish and all these cells adhered to it. Nothing further was noticed even though we watched it for nearly half an hour subsequently. From this and other observations we think that the intermediate forms are not only efficient phagocytes (*sensu restricto*) of the malarial

parasites, but are also responsible for their destruction.

Function of monocytes

The absence of any debris, other than a few particles of malarial pigment, from these cells suggests that the true monocytes are poor phagocytes as compared with the histiocytes. (Admittedly this might indicate that they digest the parasites so quickly that they are never seen to contain them in supra-vital-stained preparations; we do not however take this view.) Thus, the claim for the function of monocytes in malarial immunity is dependent on the evidence of their response to the invasion of the parasites which we have clearly demonstrated (*vide supra*) and—if we accept the suggestion that the intermediate forms arise from them—on their ability to assume phagocytic powers under special conditions, also, in the absence of a good monocyte response, on the failure of a histiocyte increase alone to bring about an appreciable reduction in the parasite count. Though the figures in the other tables (I to VIII) do not bring out the fact very clearly we have other evidence which indicates that a continued high monocyte response, as is seen in certain monkeys in which the infection becomes chronic (or latent), even in the absence of a high histiocyte count, will control the infection and prevent any increase in parasites. Table IX demonstrates the importance of this monocyte response in malarial immunity very clearly.

We therefore assume that the action of monocytes is an indirect one, and that the increase in the number of monocytes is associated with some change in the plasma which produces a reduction in the number of parasites. What exactly is the nature of the change in the plasma, or how it produces this effect, we will not attempt to suggest.

We have gained an impression—which subsequent investigations may support or disprove—that there is slowing down of the sexual cycle when this monocytosis is evident. In any case, there is, we think, ample evidence that monocytosis is an important factor both in resistance and cure.

Conclusions

It is apparent from the above-recorded observations that each of the three types of mononuclear cell plays a part in malarial immunity. The function of the histiocyte is primarily the removal of damaged red cells from the peripheral blood. In a malarial attack it is the first cell to be stimulated—the stimulus probably coming from the red-blood-cell debris resulting from the early schizogony cycles. As more and more red cells are destroyed the histiocyte percentage rises, and it falls again when the infection becomes latent and there is little blood destruction occurring. In those cases in which the infection gains the upper hand and there is a general failure of cellular response,

the histiocyte percentage also falls. The destruction of malarial parasites by these cells may be only incidental, but the number they remove from the circulation must be considerable.

The intermediate type is the next cell to be stimulated and here again it may be the demand for the removal of cell debris which has called for their presence in large numbers in the peripheral blood, or has stimulated monocytes to assume increased phagocytic activity. These cells destroy a large number of parasites, their lytic properties seem to be much greater than those of the histiocytes, as the parasites they contain always appear to be in an advanced stage of disintegration.

The monocyte is the last cell to be stimulated and we have suggested that the origin of this stimulus is the destruction of a number of malarial parasites in the early stages of the infection by the reticulo-endothelial cells, the histiocytes. As long as there are any malarial parasites present in the body the monocyte count will remain high, except in those cases in which there is a general failure of cellular response which precedes the death of the animal, and conversely as long as the monocyte count remains high the malarial infection will not get the upper hand. The action of the true monocyte in malarial immunity is probably indirect and is associated with some humoral change in the serum which limits the multiplication of the parasites in the body.

There is considerable evidence to show that in malarial infection quinine acts partly by stimulating the normal processes of cellular immunity.

Summary

1. Over 300 specimens of blood from 18 monkeys (12 *Macacus mulatta* and 6 *M. irus*) were studied with the help of the supra-vital staining technique.

2. The large mononuclear cells present in the blood during the pre-patent, patent, latent and secondary patent periods, as well as the period following the administration of quinine, were studied and classified as either monocyte, histiocyte or an intermediate type.

3. From the results obtained, the probable function of monocytes and histiocytes in the cure of malaria is discussed, and certain tentative conclusions are arrived at.

4. *Camera-lucida* drawings of some of the typical monocytes and histiocytes found in the peripheral blood of monkeys in the course of the present investigation are given in a coloured plate.

Acknowledgment

Our thanks are due to Mr. Mullick for the patience and care he exercised in the preparation of the coloured plate.

All the blood counts in this series were done by the first two workers; all three workers are responsible for the presentation of the results and for the conclusions.

REFERENCES

Napier, L. Everard, and Campbell, H. G. M. (1932). Observation on a Plasmodium Infection which causes Hæmoglobinuria in Certain Species of Monkey. *Indian Med. Gaz.*, LXVII, p. 246.

Napier, L. Everard, Krishnan, K. V., and Lal, Chiranji [(1932) and (1932a)]. Cytological Studies of the Blood and Tissues in Kala-azar and Associated Conditions. Part III: Large Mononuclear Cells in Human Malaria, and Part I: Supra-vital Staining Technique. *Indian Med. Gaz.*, LXVII, p. 135 and p. 251.

APPENDIX

Tables showing the percentage distribution of the different types of large mononuclear cells in the blood of normal monkeys and of monkeys in different stages of a malarial attack.

TABLE I

Normal monkeys, prior to inoculation

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	25,000	6	5	1	0
	13,750	5	4	1	0
	10,000	5	5	0	0
	16,875	5	5	0	0
	14,000	4	4	0	0
	15,000	4	4	0	0
	9,000	4	3	1	0
	17,500	4	4	0	0
	15,000	4	4	0	0
	16,875	3	2	1	0
Mean	15,300	4.4	4	0.4	0
<i>M. irus</i>	16,875	3	3	0	0
	14,000	4	4	0	0
	17,500	5	5	0	0
	18,750	4	4	0	0
	15,000	4	4	0	0
	12,000	5	4	1	0
Mean	15,688	4.2	4	0.2	0

TABLE II

During the pre-patent period, a few days prior to the finding of the parasites in the blood

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	10,000	3	3	0	0
	14,375	3	1	1	1
	15,625	6	5	1	0
	16,875	5	5	0	0
	11,250	5	2	2	1
	9,000	4	3	1	0
	14,000	5	4	0	1
	13,750	5	3	1	1
	15,000	5	2	1	2
Mean	13,319	4.6	3.1	0.8	0.7
<i>M. irus</i>	17,500	6	3	2	1
	18,750	6	2.5	2.5	1
	18,750	6	3	2	1
	18,000	6	2	3	1
	16,250	5.5	3	2	0.5
Mean	17,850	5.9	2.7	2.3	0.9

TABLE III

On the first day of the patent period

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	10,000	6	2	2	2
	14,000	4	1	1	2
	15,000	6	5	1	0
	10,000	6	2	1	3
	11,250	8	1.5	1.5	5
	17,500	13	1.5	2.5	9
	16,250	8	1	2	5
	11,000	4	1	2	1
	16,000	6	1	3	2
Mean	13,444	6.8	1.8	1.8	3.2
<i>M. irus</i>	10,000	7	4	1	2
	25,000	16	12	4	0
	13,000	7	2	2	3
	15,625	9	6	2	1
	17,500	8	6	2	0
Mean	16,225	9.4	6	2.2	1.2

TABLE IV

About the middle of the patent period when the animals were not looking very ill even though the parasite count was fairly high

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	15,000	6	2	2	2
	22,000	8	2	4	2
	18,750	10	5	3	2
	16,875	8	2	4	2
	13,000	17	3	8	6
	16,875	9	1	5	3
	17,500	8	2	4	2
	20,000	18	4	10	4
	21,000	20	2	10	8
	13,750	13	1	8	4
	20,000	14	3	9	2
	16,875	12	2	7	3
	17,500	15	5	6	4
	11,500	8	2	4	2
	14,000	9	3	5	1
	15,000	9	4	5	0
Mean	16,852	11.5	2.7	5.9	3.0
<i>M. irus</i>	11,000	9	4	3	2
	12,500	9	3	2	4
	13,000	12	3	6	3
	25,000	10	4	3	3
	18,000	9	5	2	2
	23,400	12	4	6	2
	22,500	10	2	3	5
	16,000	9	4	2	3
Mean	17,675	10.0	3.6	3.4	3.0

TABLE V

When the animals were ill and the parasite rate high

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	15,000	7	2	2	3
	12,000	8	2	4	2
	19,375	6.5	1.5	3.5	1.5
	15,625	9	6	2	1
	17,500	8	2	4	2
	15,000	9	2	5	2
	21,000	6	1.5	3	1.5
	11,500	8	2	4	2
	16,000	6	1	3	2
	13,000	5	1.5	2.5	1
	15,000	9	4	5	0
	6,250	7	3	3	1
	11,000	9	3	2	4
	17,000	10	3	4	3
	16,250	7	1	4	2
	13,000	6	2	3	1
Mean	14,656	7.5	2.4	3.4	1.8

TABLE VI

Twelve to 36 hours before death due to a severe and rapidly progressing infection

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	13,000	3.5	1.5	1	1
	10,000	4	1.5	1.5	1
	14,000	3	1	1	1
	10,000	6	0	1	5
	20,000	6	1.5	3	1.5
	15,000	6	2	2	2
	19,000	6	1.5	3	1.5
	13,000	5	1.5	2.5	1
Mean	14,250	5	1.3	1.9	1.8

TABLE VII

One to two days after the administration of quinine which resulted in the complete or partial disappearance of the parasites from the peripheral blood (to be compared with table V)

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	20,000	10	3	3	4
	13,750	10	4	4	2
	19,375	8	2	4	2
	21,875	11	2	4	5
	16,000	10	4	3	3
	16,000	8	3	4	1
	17,000	9	2	5	2
	14,000	18	4	10	4
	13,000	9	4	2	3
	18,000	12	3	4	5
	15,000	9	2	5	2
	18,000	18	6	6	6
	16,250	14	4	4	6
	17,000	18	5	5	8
	13,000	18	4	7	7
	15,000	12	4	3	5
	17,500	8	2	3	3
	19,000	8	2	2	4
	18,000	20	6	6	8
	11,300	14	6	3	5
	9,000	10	6	2	2
Mean	16,098	12.1	3.8	4.2	4.1
<i>M. irus</i>	15,000	19	8	6	5
	19,000	15	7	6	2
	20,000	20	7	5	8
	22,000	19	6	7	6
Mean	19,000	18.3	7	6	5.3

TABLE VIII

A few days prior to the onset of latency due to natural causes and without the administration of quinine (to be compared with table IV)

	Number of leucocytes per c.mm.	PERCENTAGES OF			
		total large mono-nuclears	mono-cytes	inter-mediate forms	histio-cytes
<i>M. mulatta</i>	19,000	20	5	7.5	7.5
	17,500	17	5	6	6
Mean	18,250	18.5	5	6.8	6.8
<i>M. irus</i>	26,000	12	5	3	4
	17,000	10	3	4	3
	14,000	10	5	2	3
	16,250	13	4	5	4
	15,000	19	8	6	5
	20,000	14	3	9	2
	21,200	16	12	3	1
	22,000	17	8	7	2
	19,000	15	7	6	2
	15,000	16	4	8	4
	13,000	17	3	8	6
Mean	18,041	14.5	5.6	5.6	3.3

DESCRIPTION OF PLATE I

Cytological studies of the blood and tissues in kala-azar and associated conditions.

PARTS IV AND V.

Figures 1 to 16 in this plate are cells from supra-vitally stained preparations of the blood of monkeys suffering from malaria, and figures 17 to 27 are cells from the peripheral blood and spleen of human kala-azar cases. The drawings were made from *camera-lucida* sketches; in order to ensure correct colouring, fresh microscopic specimens were used as a guide.

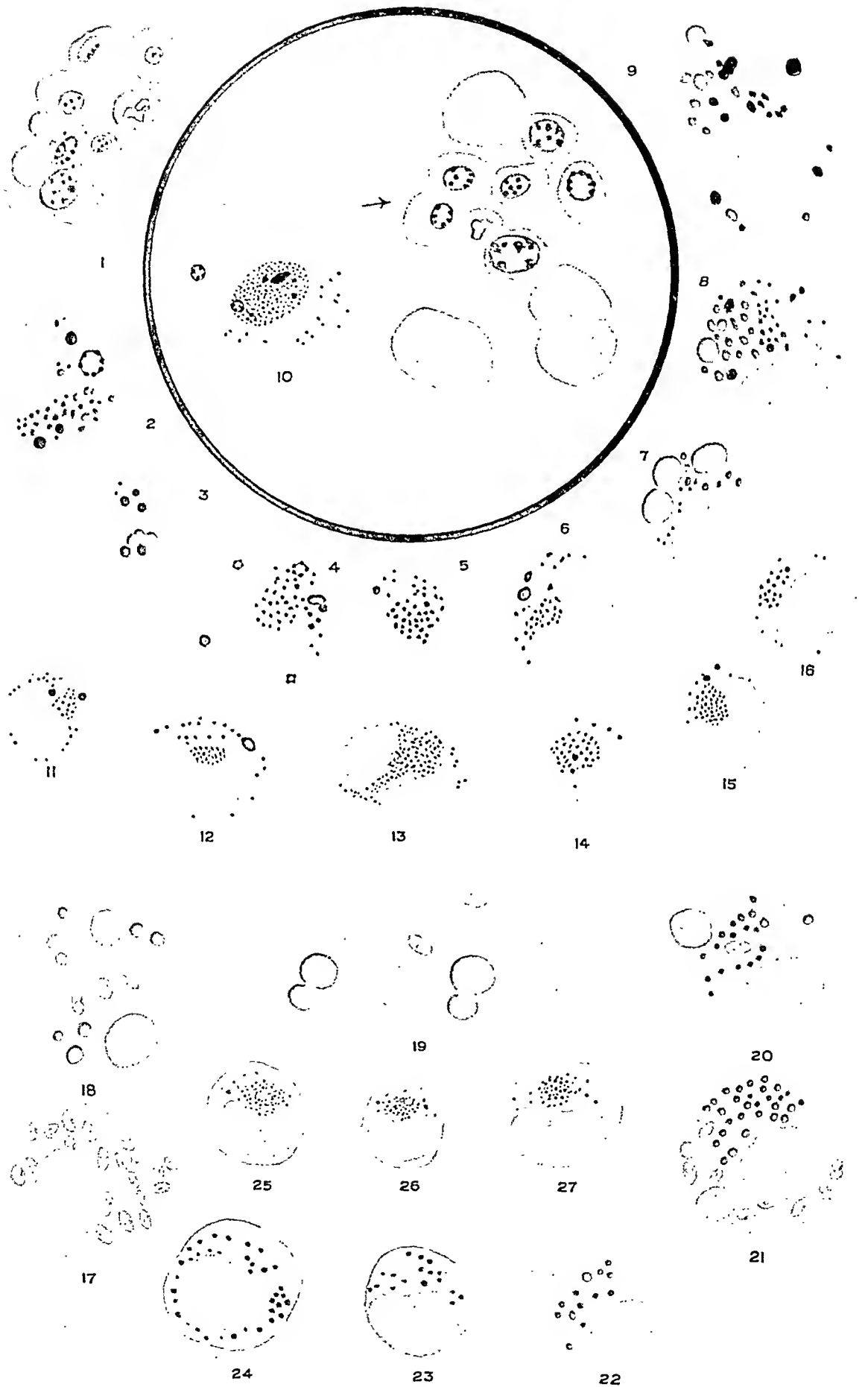
PART IV. *The large mononuclear cells in monkey malaria.*

1. A histiocyte showing a number of infected red cells and a disintegrating malarial parasite.
2. A histiocyte with pigment and malarial parasite.
3. A histiocyte with malarial pigment.
- 4, 5 and 6. Intermediate forms with malarial pigment. No. 4 in addition shows malarial parasites.
7. A histiocyte showing a few mitochondria and large neutral-red vacuoles.
- 8 and 9. Histiocytes with malarial pigment. No. 8 shows also a few mitochondria.
10. An intermediate form that was seen actively moving towards a collection of infected red cells. Note the round area at the *hof* of the nucleus. This and the mitochondria led us to classify this cell as an intermediate form, though it is an unusually large one. It was in the vacuole-like area that the cell segregated the ingested substances first, and, later, after digesting them, sent them to the periphery.
- 11 and 12. Monocytes with malarial pigment.
13. A monocyte in the process of cell division.
- 14, 15 and 16. Forms intermediate between monocytes and our intermediate forms, classified as monocytes, showing malarial pigment.

PART V. *The large mononuclear cells in the peripheral and in the spleen blood in kala-azar.*

17. A histiocyte from spleen with many *Leishmania donovani*—although actively phagocytic it shows a preference for parasites only.
- 18 to 21. Histiocytes from spleen showing *L. donovani*, neutral-red vacuoles and red blood cells. No. 19 in addition shows an ingested nucleus. All these cells were actually seen ingesting the red cells and *Leishmania* that were present in their immediate neighbourhood.
- 22 to 24. Histiocytes from peripheral blood. No. 24 was the common type seen in kala-azar and it is peculiar in that the distribution of neutral red is all round the nucleus instead of in the area in front of it.
- 25 and 26. Monocytes from peripheral blood. In addition to the rosette a tiny vacuole or two of neutral red is also present.
27. A monocyte from the spleen.

PLATE I.



CYTOLOGICAL STUDIES OF THE BLOOD AND TISSUES IN KALA-AZAR AND ASSOCIATED CONDITIONS

Part V.

THE LARGE MONONUCLEAR CELLS IN THE PERIPHERAL AND IN THE SPLEEN BLOOD IN KALA-AZAR.

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From time to time conflicting opinions have been expressed by different workers regarding the rôle of the phagocytic large mononuclear cells in kala-azar. Knowles (1920) suggested that the hyaline cells of the blood function as host cells rather than as destroyers of leishmania. Brahmaehari (1928) stated that the development of *clasmatocytes* is what one should aim at in the treatment of kala-azar, thereby presumably meaning that these cells are destructive, rather than protective, to leishmania. Cash and Hu (1927) as a result of their cytological studies on leishmania-infected hamsters came to the conclusion that increase of *clasmatocytes* favours multiplication of leishmania and helps in the distribution of the parasites to the different parts of the body. Krishnan (1932) from his studies of the leucocyte changes in human kala-azar, stated that the cells of the reticulo-endothelial system were responsible both for susceptibility and resistance, and that increase in the number of phagocytic cells without destructive powers favoured infection. From these references it will be clear that as yet no definite decision has been arrived at regarding the part played by the two different types of large mononuclear cell, the monocyte and the histiocyte, in kala-azar. As we are of opinion that a knowledge of the cellular and serological conditions favourable to invasion of leishmania would be of great value at the present stage of the kala-azar transmission problem, we investigated the cellular changes in the large mononuclear group in the blood and tissues of kala-azar cases with the help of the supra-vital staining technique.

The large mononuclear cells in the peripheral blood in kala-azar

The subjects of this study were kala-azar patients in the wards of the Carmichael Hospital for Tropical Diseases. They were all diagnosed as kala-azar by the demonstration of the parasite in their peripheral or spleen blood, either by direct examination of a stained smear or by cultural methods. The patients were mostly Indian adult males who had hitherto had no specific treatment for kala-azar. A few, including two of the patients who did not respond to treatment, had previously been treated for the disease and had relapsed, but none of these

had received any antimony injections for at least two months prior to the commencement of the present investigation of their blood cellular condition.

The treatment given was that which has for some time been adopted as the routine treatment for kala-azar in our hospital, namely, daily intravenous injections of neostibosan, commencing with a dose of 0.3 gramme and making 0.5 gramme the maximum: during part of the investigation only six doses were given, but later the total number was increased to eight. No difference was observed clinically, or otherwise, in the results obtained with these two different courses of treatment.

The supra-vital staining technique and the criteria for identification of the different cells are those which have already been described by the present writers in previous papers in this series. The large mononuclear cells were classified as monocytes (including the intermediate forms*) or histiocytes.

Altogether 322 samples of peripheral blood from 59 cases of kala-azar were studied. Of these 96 samples were obtained prior to treatment, 72 samples during treatment, and 154 samples from 1 to 4 weeks after completion of treatment.

For tabulation of the results, patients have been divided into two groups, those who did and those who did not improve clinically; and the latter group has again been divided, as far as after-treatment counts are concerned, into those cases in which there was a total leucocyte increase and those in which there was no such increase.

TABLE A
Patients that were successfully treated

Total leucocytes per c.mm.	Mean of counts	Probable error of mean	Range of counts
(i) Prior to treatment; 88 counts in 44 cases.			
Total leucocytes per c.mm.	3,620	± 112.27	2,000 to 6,000
Total large mononuclear percentage.	9.55	± 0.27	4 to 18
Monocyte percentage	3.85	± 0.16	1 to 8
Histiocyte percentage	5.69	± 0.22	2 to 10
Ratio M/H $\times 100$	73.61	± 5.26	14 to 350
(ii) At conclusion of course of injections; 46 counts in 46 cases.			
Total leucocytes per c.mm.	4,926	± 160.4	2,500 to 7,500
Total large mononuclear percentage.	8.38	± 0.24	5 to 13
Monocyte percentage	5.86	± 0.19	4 to 9
Histiocyte percentage	2.52	± 0.14	1 to 5
Ratio M/H $\times 100$	255.44	± 11.55	100 to 400

*Our reason for not differentiating between intermediate forms and monocytes in this series is that some of the counts were made at the beginning of these 'supra-vital' investigations, at a time when this differentiation was not made, so that, to bring all the counts into line, it was necessary to group the monocytes and intermediate forms together in the whole series.

TABLE A—concl'd

Total leucocytes per c.mm.	Mean of counts	Probable error of mean	Range of counts
(iii) 2 to 4 weeks after completion of treatment; 126 counts in 54 cases.			
Total leucocytes per c.mm.	7,040	± 155.25	3,100 to 12,500
Total large mononuclear percentage.	7.84	± 0.18	4 to 15
Monocyte percentage	6.15	± 0.17	3 to 12
Histiocyte percentage	1.69	± 0.07	1 to 5
Ratio M/H × 100	433.73	± 17.08	100 to 1,000

(iv) At time of discharge as cured; 16 counts in 16 cases.

Total leucocytes per c.mm.	5,025	± 344.29	3,000 to 7,500
Total large mononuclear percentage.	4.41	± 0.21	3 to 6
Monocyte percentage	4.41	± 0.21	3 to 6
Histiocyte percentage	0
Ratio M/H × 100

TABLE B

Patients that showed little or no improvement after treatment

Total leucocytes per c.mm.	Mean of counts	Probable error of mean	Range of counts
(i) Prior to treatment; 8 counts in 5 cases.			
Total leucocytes per c.mm.	3,275	± 185.33	2,500 to 4,000
Total large mononuclear percentage.	13.19	± 1.06	8 to 18
Monocyte percentage	4.32	± 0.43	3 to 6
Histiocyte percentage	8.87	± 0.97	5 to 12
Ratio M/H × 100	49.5	± 2.22	43 to 60

(ii) 1 to 4 weeks after completion of treatment in cases showing no increase of leucocytes; 26 counts in 3 cases.

Total leucocytes per c.mm.	3,638	± 130.58	2,500 to 5,000
Total large mononuclear percentage.	9.17	± 0.49	4 to 14
Monocyte percentage	3.64	± 0.29	2 to 7
Histiocyte percentage	5.53	± 0.39	2 to 10
Ratio M/H × 100	77.07	± 7.44	20 to 167

(iii) 1 to 4 weeks after completion of treatment in cases showing increase of total leucocytes; 12 counts in 2 cases.

Total leucocytes per c.mm.	7,200	± 162.77	6,300 to 8,100
Total large mononuclear percentage.	6.77	± 0.83	5 to 11
Monocyte percentage	1.49	± 0.66	1 to 2
Histiocyte percentage	5.28	± 0.54	3 to 9
Ratio M/H × 100	33.5	± 4.59	17 to 67

The results of the peripheral blood counts recorded above, bring out the following points:—

(1) In kala-azar there is a marked increase in the large mononuclear elements in the peripheral blood. This increase, as judged by the

mean of the observations, is slightly more marked in those cases which subsequently do not improve on treatment, but the deviation from the mean is a wide one and the difference is not large enough to make this observation one of prognostic significance.

The feature of this mononuclear increase is a marked histiocyte increase; these cells may number 12 per cent. of the total white count and are much more numerous in the cases with a bad prognosis. The monocyte/histiocyte ratio is nearly always below 1.

(2) With the commencement of specific treatment there occurs a distinct drop in the relative number of histiocytes and a rise in the number of monocytes. When the patient is progressing towards recovery these changes are very much more pronounced, and eventually the ratio of monocytes to histiocytes is completely reversed.

(3) If, however, treatment fails to bring about cure, neither the drop in histiocytes nor the rise in monocytes is noticeable.

(4) In all the cases of the first group, i.e., those which respond well to treatment, there is a marked increase in the total leucocyte count after treatment: in some of the cases of the other group there is also a leucocyte increase, but in these cases there is no reversal of the monocyte/histiocyte ratio. This seems to be an essential reaction for cure to be effected.

The large mononuclear cells in the spleen blood in kala-azar

Although usually a study of the peripheral blood gives a very good indication of the pathological and immunological changes taking place within the body, it was thought that it was important also to study the blood cellular changes taking place in an actual focus of infection such as the spleen. For, in this disease the characteristic change is an increase in the number of histiocytes and these are at times of enormous size, reaching 100 to 150 μ in diameter, and, being so large, are liable to be caught up in the lung capillaries and to get no chance to enter the peripheral circulation. Simpson (1922) and we ourselves have observed that in certain experimental rabbits proliferation of histiocytes resulting from repeated injections of colloidal dyes was not always accompanied by a corresponding increase of these cells in the peripheral blood. For this reason a study of the large mononuclear changes in the spleen was undertaken with the hope that it would furnish more conclusive and significant data than the study of the peripheral blood alone.

The blood was obtained from the spleen by the ordinary spleen puncture technique. A dry sterilized all-glass syringe was used, with the spleen puncture attachment (Napier, 1928) which enables the syringe to be manipulated with one hand while the other is used to control the spleen. Though it was not necessary to

maintain suction until blood appeared in the barrel of the syringe, it is necessary to withdraw and release the plunger rather more often than in ordinary routine puncture, as a large drop of blood is necessary for making two supra-vital preparations, whereas for diagnostic purposes the merest trace of blood is all that is necessary. This necessity to obtain a sufficiency of material prolongs and theoretically adds to the danger of the operation; we say 'theoretically' because we did not in these cases observe any increase in the post-spleen-puncture pain, which occurs occasionally and which can be attributed to local trauma, and in no case did more serious symptoms follow. For this reason we did not usually perform a spleen puncture more than twice and never more than three times on the same patient.

Incidentally, these spleen punctures demonstrated how infrequently one obtains what is usually described as 'spleen pulp' in this operation. In nine cases out of ten the material obtained spreads as quickly and as homogeneously under the coverslip as ordinary peripheral blood; it is in fact blood from the small sinusoidal spaces admixed with a very little fine cellular debris from the damaged spleen parenchyma. The blood which sometimes rushes into the syringe during a spleen puncture is from one of the larger splenic venous spaces. In either case the cellular composition of the blood is different from that of the peripheral blood which has subsequently passed through at least two sets of capillaries. The little granules of pulp which one sees in spleen-puncture material and which some writers have described as the *sine qua non* of a good spleen puncture are usually the result of an error in technique, either leaving some antiseptic in the barrel which coagulates the blood, or delaying too long before expressing the blood, which clots unusually rapidly.

A few preliminary experiments with spleen puncture material showed us that certain modifications in the usual procedure would have to be adopted before adequate data could be obtained from a study of it. First of all, on account of the very small amount of spleen blood that was generally obtainable by puncture, it was not possible to do a quantitative estimation of the white cells; even in the few instances where there was sufficient blood, whilst the supra-vital preparations were being made, the blood usually clotted in the syringe and thus became useless for cell enumeration. Secondly, when more than one puncture was done on the same patient on the same occasion—a practice that could only be adopted in certain cases—and cell counts performed on the different samples, it was noticed that very varying results were obtained. It is natural that there should be considerable discrepancies in samples taken from the small splenic sinuses, and from large venous spaces; the differences were at times so considerable that we were

convinced that total counts were valueless; on two or three occasions the point of the needle had obviously rested in a Malpighian corpuscle as the whole preparation was swamped by small lymphocytes; such preparations were discarded. With regard to the large mononuclear cells, however, the ratio between the monocytes and the histiocytes remained fairly constant in all the samples, and was not subject to any appreciable sampling error. Therefore, we decided to record our observations as variations in the ratio between these two cells; this nearly always corresponds closely with the ratio in the peripheral blood.

We made not less than two supra-vital preparations from each specimen of puncture material, counted all the large mononuclear cells in each, and from that calculated the number of monocytes and histiocytes present in 50 microscopic fields (the last procedure was adopted to facilitate statistical calculation). By this means we hoped to obtain not only a correct idea of the variation in the ratio of the two types of mononuclear cell, but also a rough idea of the quantitative changes in the total large mononuclear cells. Side by side with these examinations, fixed films of spleen blood were stained by Giemsa's stain and the number of parasites present in them estimated and grouped as +, ++, or ++++. This enabled us to correlate the cellular changes with increase or decrease of parasites.

The coloured plate, figures 17–27, shows the various cell types seen in the peripheral and spleen blood.

Altogether 59 samples of spleen puncture material were obtained in 32 cases of kala-azar. The patients were amongst those whose peripheral blood counts were made (*vide supra*). It was not possible to perform spleen puncture as often as we should have liked, as the condition of the patient had to be taken into consideration. It was therefore only in a few cases that we were able to follow up the cellular changes by punctures at the three different stages of the disease. In the majority of cases puncture was done only once at some distinct stage of infection or of recovery. Of the 59 samples examined 26 were from cases prior to treatment, 12 from cases during treatment, and 21 from cases after completion of treatment. The results obtained are given in the tables below.

The counts normally fall into three groups, *before*, *during*, and *after* treatment. There are a number of ways in which the untreated patients could be grouped, according to the acuteness of the illness, according to the length of duration of the disease, according to the size of the spleen, or according to the number of parasites present in the spleen blood. There is of course a considerable though not a complete correlation between the duration of the disease and the size of the spleen, but we found little correlation

between either these or the acuteness of the illness, and the cellular reaction; on the other hand we found a considerable correlation between the number of parasites and the cellular reaction, so that we divided our cases into two groups according to whether there were few or abundant parasites in the spleen puncture smears. Our criterion was whether there were more or less than one parasite *per field*; there was usually a sharp differentiation between the two groups of cases. It will be seen that the difference between the counts in these two groups is significant from a mathematical standpoint.

Again some patients react well clinically to treatment, others do not. We have therefore divided the treated patients into two groups according to their response to treatment, judged on clinical standards, *i.e.*, the absence of fever and the reduction in the size of the spleen. Patients of the latter group are comparatively rare but we have included as many as possible; the 8 counts were obtained from 3 such patients.

The tables are self explanatory.

The conclusions drawn from them can be summarized as follows:—

That in untreated kala-azar the monocyte/histiocyte ratio is low, always below 1 and in extreme cases below 0.1, and that it varies inversely with the intensity of the infection as demonstrated by the number of parasites in a smear.

That under treatment the monocyte/histiocyte ratio steadily increases, *pari passu* with the disappearance of the parasites and the clinical progress of the patient towards recovery; in the two extreme groups the mean ratio has undergone a 15-fold increase.

That when the patient does not improve clinically the monocyte/histiocyte ratio remains low and unchanged.

Discussion

The characteristic histological reaction in kala-azar is a marked increase of tissue histio-

TABLE C

Cellular changes in the large mononuclear group in the spleen blood in kala-azar : summary of tables I to V

Table	Group	Number of observations	MEAN OF THE			Probable error
			Numbers of monocytes in 50 fields	Numbers of histiocytes in 50 fields	Ratios M/H $\times 100$	
I	Untreated cases; few parasites.	10	7.0	11.3	62.72	± 4.04
II	Untreated cases; many parasites.	16	7.25	22.75	36.05	± 2.38
III	At end of course of injections; few parasites.	14	8.7	9.6	114.07	± 12.91
IV	Some weeks after successful treatment; no parasites.	11	19.7	4.66	507.87	± 30.50
V	Some weeks after unsuccessful treatment; few parasites.	8	6.0	18.9	35.86	± 5.07

TABLE D

Statistical analysis and comparison of different groups

Groups compared	Difference between the means of the two groups	Probable error of the difference	REMARKS
I & II	26.67	± 4.69	Significant.
I & III	51.35	± 13.52	Almost significant.
I & IV	445.15	± 30.75	Certainly significant.
II & IV	471.82	± 30.59	Certainly significant.
II & V	0.19	± 5.41	Not significant.

cytes at the various foci of infection; these foci are in many parts of the body wherever reticulo-endothelial cells are to be found, but most characteristically in the spleen. It is generally accepted that this increase in the number of histiocytes is caused by local multiplication, but the evidence of this is incomplete. We have shown above that together with this local aggregation of tissue histiocytes there is an increase in the number of histiocytes in the blood in the sinusoidal spaces of that reticulo-endothelial sponge, the spleen. Some of these histiocytes find their way into the general blood stream and the smallest of them eventually reach the peripheral blood where, we have also shown, they are to be found in relatively large

numbers, both parasitized and unparasitized. The immediate result of treatment is to reduce the focal aggregation of tissue histiocytes (this is reflected clinically by an early reduction in the size of the spleen); from our cytological studies we have no evidence of the fate of these cells. The evidence that they are carried away in the blood is lacking, as we have never noticed even a temporary increase of these cells in either the spleen or peripheral blood; on the contrary, there was an early marked decrease in the histiocytes of the spleen blood, as well as of peripheral blood. The assumption is therefore that local disintegration occurs. Together with this histiocyte decrease there is a monocyte increase; this is equally apparent in both the spleen and the peripheral blood.

To summarize, it appears that the characteristic reaction to leishmania infection is a histiocytosis, both focally and in the peripheral blood, and that the characteristic cellular reaction of successful immunity response is a monocytosis. The monocyte is not a very active phagocyte, so that we must conclude that the increase in the numbers of this cell in the blood is associated with a specific humoral reaction.

Observations bearing on the relationship of kala-azar and malaria

In both the blood and the tissue histiocytes there is little sign of 'digestion' of the leishmania and on the contrary there is evidence of free multiplication. This reaction of the host is therefore not in any way an immunity response but is probably a non-specific, purely cellular reaction to the presence of foreign bodies, and we know from clinical experience that there is little tendency, when a visceral infection is once established, for spontaneous recovery to take place without the intervention of some severe infection, such as pneumonia.

Furthermore, it seems quite possible that the histiocyte proliferation which occurs during a malarial attack (see previous papers in this series) would tend to disseminate and provide suitable nidi for a hitherto localized leishmania infection.

On the other hand we have shown that the histiocyte is capable of phagocytosing and destroying malarial parasites contained in red blood cells and we have suggested that such action might check a malarial infection. There is considerable evidence that this histiocyte reaction is a non-specific one. Thus the histiocyte response which occurs in kala-azar may be the factor responsible for keeping down the malarial infection in a kala-azar patient. (It is an indisputable fact and one to which the senior writer has repeatedly drawn attention that malarial parasites are rarely found in the blood of a kala-azar patient, but that again and again when the kala-azar is cured a typical clinical attack of malaria, with parasites in the peripheral blood, occurs.) It might then be argued, if a monocytosis is the characteristic

cellular reaction associated with successful immunity response, why does not the monocytosis, which is associated with a cure in kala-azar and is maintained for some considerable time, check the malarial infection also. We have already suggested that the monocyte does not act directly, but that the immunity response which effects a cure in malarial infection, though associated with a monocytosis, is of a humoral nature, and it is probably specific. Therefore, though a monocytosis is an essential factor in immunity response, specific stimulation is required before a specific immunity response to malarial infection will occur.

Acknowledgment

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REFERENCES

- Brahmachari, U. N. (1928). *A Treatise on Kala-azar*, p. 148.
 Cash, J. R., and Hu, C. H. (1927). The Clasmato-cytes in Experimental Kala-azar. *Trans. Seventh Congress, F. E. A. T. M.*, III, p. 44.
 Knowles, R. (1920). A Study of Kala-azar, Part II—Peripheral Blood in Kala-azar. *Indian Journ. Med. Res.*, VIII, p. 162.
 Krishnan, K. V. (1932). Changes in the Leucocyte Picture in Kala-azar after Adrenalin Injection and their Significance. *Indian Journ. Med. Res. Memoirs*, No. 25, p. 23.
 Napier, L. Everard (1928). A Spleen Puncture Syringe. *Indian Journ. Med. Res.*, XVI, p. 149.
 Simpson, M. E. (1922). The Experimental Production of Macrophages in the Circulating Blood. *Journ. Med. Res.*, XLIII, p. 77.

APPENDIX

Cellular changes in the large mononuclear group in the spleen blood in kala-azar

TABLE I
Untreated cases; few parasites

Serial number	Number of monocytes in 50 fields	Number of histiocytes in 50 fields	Ratio M/H $\times 100$	Probable error of ratio
1	11	12	91.66	
2	10	12	83.33	
3	6	12	50.00	
4	8	16	50.00	
5	7	11	63.63	
6	5	6	83.33	
7	10	14	71.42	
8	6	10	60.00	
9	3	8	37.50	
10	4	12	33.30	
Mean.	7	11.3	62.72	± 4.04

TABLE II
Untreated cases; many parasites

Serial number	Number of monocytes in 50 fields	Number of histiocytes in 50 fields	Ratio M/H × 100	Probable error
11	5	18	27.77	
12	10	27	37.03	
13	9	18	50.00	
14	6	12	50.00	
15	2	22	9.09	
16	6	12	50.00	
17	11	32	34.37	
18	9	18	50.00	
19	10	61	16.39	
20	8	15	53.33	
21	4	25	16.00	
22	8	25	32.00	
23	6	12	50.00	
24	5	25	20.00	
25	8	20	40.00	
26	9	22	40.90	
Mean.	7.25	22.75	36.05	± 2.38

TABLE III
At end of course of injections; few parasites

Serial number	Number of monocytes in 50 fields	Number of histiocytes in 50 fields	Ratio M/H × 100	Probable error
27	6	6	100.00	
28	8	12	66.66	
29	8	18	44.44	
30	17	14	121.40	
31	7	11	63.63	
32	12	4	300.00	
33	9	6	150.00	
34	4	16	25.00	
35	6	7	85.71	
36	10	12	83.33	
37	4	9	44.44	
38	11	8	137.50	
39	6	3	200.00	
40	14	8	175.00	
Mean.	8.7	9.6	114.07	± 12.91

TABLE IV
Some weeks after successful treatment; no parasites

Serial number	Number of monocytes in 50 fields	Number of histiocytes in 50 fields	Ratio M/H × 100	Probable error
41	22	15	146.66	
42	25	4	625.00	
43	12	4	300.00	
44	32	5	640.00	
45	10	2	500.00	
46	12	2	600.00	
47	12	2	600.00	
48	30	5	600.00	
49	10	2	500.00	
50	27	6	450.00	
51	25	4	625.00	
Mean.	19.7	4.66	507.87	± 30.50

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ON THE THERAPEUTIC VALUE OF THIO-SARMINE IN THE TREATMENT OF SYPHILIS

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THE voluntary venereal hospital in Calcutta is the only government institution in India for the treatment exclusively of venereal diseases; only women are admitted here.

In this paper an attempt has been made to study the effect of thio-sarmine which is prepared in the Brahmachari Research Institute, Calcutta, for the treatment of syphilis.

The compound thio-sarmine is sulph-arsenobenzene or di-sodium-dioxy-diamino-arsenobenzene-methylene sulphonate, and is allied to sulfarsenol, kharsulphan, sulpharsphenamine, sulphostab, etc. It is a light yellowish powder readily soluble in water. The solution used is made with distilled water freshly boiled before use and cooled. The solution is injected immediately after preparation. We have used 10 to 20 per cent. solutions which are slowly injected either subcutaneously or intramuscularly into the deltoid or buttocks twice in a week.

Generally we begin the treatment with a dose of 0.3 gramme and gradually increase the dose up to 0.6 gramme and the average total amount of 5.1 grammes was administered to each patient. During the treatment the intermediate doses were repeated, if found desirable.

The toxicities of thio-sarmine, sulfarsenol, sulpharsphenamine are almost the same in experimental animals. Given intravenously the maximum tolerated dose of thio-sarmine = 300 milligrammes, majority tolerated dose = 360 milligrammes, and the minimum lethal dose

(Continued from previous column)

TABLE V
Some weeks after unsuccessful treatment; few parasites

Serial number	Number of monocytes in 50 fields	Number of histiocytes in 50 fields	Ratio M/H × 100	Probable error
52	5	19	26.33	
53	8	14	57.14	
54	5	26	19.23	
55	10	12	83.33	
56	6	18	33.33	
57	5	22	22.72	
58	4	19	21.05	
59	5	21	23.89	
Mean.	6	18.9	35.86	± 5.07

= 490 milligrammes, per kilogramme of body weight, in the case of white rats.

Cases which gave positive Wassermann reactions and showed syphilitic manifestations, either local or general or both, at the commencement of treatment were treated with the drug. The blood of each case was examined for Wassermann reaction before, and two to three months after completion of treatment.

The therapeutic value of the drug was proved by the disappearance of syphilitic manifestations and by the Wassermann reaction remaining negative after completion of treatment.

The total number of cases treated by thio-sarminine was 30; of these 23 gave a strongly-positive Wassermann reaction and 7 a moderately-positive reaction. They were all cases of secondary syphilis.

conditions markedly improved in all the cases. Reactions, such as diarrhoea, headache, gastritis, dermatitis were not observed in any of the cases during treatment. For effects on the Wassermann reaction see table I.

We made a comparative study of the value of thio-sarminine in the treatment of syphilis by using the following drugs:—

- I. Sulfarsenol.
- II. Sulfarsenol and bismostab.
- III. Novarsenobillon.
- IV. Novarsenobillon and bismostab.
- V. Novarsenobillon and mereurosol.
- VI. Stabilarsan.
- VII. Thio-bismol.
- VIII. Quino-ido-bismuth.
- IX. Bismuth-idol.

TABLE I

Table showing treatment with thio-sarminine intramuscularly and subcutaneously and its effect on Wassermann reaction in 30 cases

Case number	DOSES IN GRAMMES			Total number of injections	Total quantity injected in grammes	Duration of treatment, in months.	WASSERMANN REACTION	
	0.3	0.45	0.6				Before treatment	After treatment
1	1	2	7	10	5.4	2 months	Strongly positive.	Strongly positive.
2	2	4	6	12	6.0	2½ "	Do.	Do.
3	1	2	7	10	5.4	2 "	Do.	Moderately positive.
4	1	4	5	10	5.1	2½ "	Do.	Do.
5	1	4	6	11	5.7	2½ "	Do.	Do.
6	1	4	5	10	5.1	2 "	Do.	Do.
7	1	4	5	10	5.1	2 "	Do.	Doubtful.
8	1	4	4	9	4.5	2 "	Do.	Do.
9	1	2	3	6	3.0	1½ "	Do.	Do.
10	2	2	3	7	3.3	1½ "	Do.	Do.
11	1	4	5	10	5.1	1½ "	Do.	Negative.
12	1	4	5	10	5.1	2½ "	Do.	Do.
13	2	4	..	6	2.4	1½ "	Do.	Do.
14	1	4	5	10	5.1	1½ "	Do.	Do.
15	2	5	2	9	4.5	2 "	Do.	Do.
16	1	2	2	5	2.4	1½ "	Do.	Do.
17	1	2	2	5	2.4	1½ "	Do.	Do.
18	1	2	4	7	3.6	1½ "	Do.	Do.
19	1	2	7	10	5.4	2 "	Do.	Do.
20	1	2	4	7	3.6	1½ "	Do.	Do.
21	2	4	4	10	4.8	2 "	Do.	Do.
22	1	2	7	10	5.4	2 "	Do.	Do.
23	1	2	7	10	5.4	2 "	Do.	Do.
24	1	4	2	7	3.3	1 month	Moderately positive.	Doubtful.
25	2	2	4	8	2.7	1 "	Do.	Do.
26	2	2	3	7	3.3	1 "	Do.	Do.
27	2	2	3	7	3.4	1 "	Do.	Do.
28	1	4	5	10	5.1	1½ months	Do.	Negative.
29	1	4	3	8	3.9	1½ "	Do.	Do.
30	2	4	..	6	2.4	1 month	Do.	Do.

Results of treatment.—The ulcers when present healed up quickly, condylomatous and elephantoid conditions disappeared gradually, adenitis subsided in the majority of cases and in those which had no suppurative eruptions over the body disappeared, and the general

The symptoms of the cases treated by these drugs were more or less the same as in those treated with thio-sarminine and consisted of hard chancre, phagedenic sore, condylomata, elephantoid condition, adenitis, arthritis, secondary eruptions, cauliflower-like growths, gummatous

sore, iritis, keratitis, etc. A comparative statement of the effects of these drugs on the Wassermann reaction is given in tables II and III.

I. *Sulfarsenol*.—Total number of cases treated was 30; of these 19 gave a strongly-positive Wassermann reaction and 11 a moderately-positive reaction. Doses—12 centigrammes, 18 centigrammes and 24 centigrammes; two injections of each dose were given to each patient either intramuscularly or subcutaneously into the buttocks in 1½ months. In our experience, higher doses of sulfarsenol are not tolerated by the patients.

II. *Sulfarsenol and bismostab*.—Total number of cases treated was 10; of these 7 gave a strongly-positive Wassermann reaction and 3 a moderately-positive reaction. Doses of sulfarsenol—12 centigrammes, 18 centigrammes and 24 centigrammes; two injections of each dose were given intramuscularly or subcutaneously, and 6 injections of 0.5 cubic centimetre dose of bismostab were given intramuscularly to each patient alternately with the former in 2½ months. In our experience, higher doses of sulfarsenol and bismostab are not tolerated by the patients.

III. *Novarsenobillon*.—Total number of cases was 30; of these 27 gave a strongly-positive Wassermann reaction and 3 a moderately-positive reaction. Doses—0.3 gramme and 0.45 gramme; 4 injections of each dose were given intravenously to each patient in two months. In our experience, higher doses of novarsenobillon are not tolerated by the patients.

IV. *Novarsenobillon and bismostab*.—Total number of cases was 30; of these 28 gave a strongly-positive Wassermann reaction and 2 moderately-positive reaction. Doses of novarsenobillon—0.3 gramme and 0.45 gramme; 4 injections of each dose were given intravenously and 8 injections of 0.5 cubic centimetre dose of bismostab were given intramuscularly to each patient, alternately with the former in 2½ months. In our experience, higher doses of novarsenobillon and bismostab are not tolerated by the patients.

V. *Novarsenobillon and mercurisol*.—Total number of cases treated was 30; of these 27 gave a strongly-positive Wassermann reaction and 3 a moderately-positive reaction. Doses of novarsenobillon—0.3 gramme and 0.45 gramme; 4 injections of each dose were given intravenously and 8 injections of 1 cubic centimetre dose of mercurisol were given intramuscularly to each patient alternately with the former in 2½ months. In our experience, higher doses of novarsenobillon and mercurisol are not tolerated by the patients.

VI. *Stabilarsan*.—Total number of cases treated was 30; of these 27 gave a strongly-positive Wassermann reaction and 3 a moderately-positive reaction. Doses—0.3 gramme and 0.45 gramme; 3 injections of each dose were given to each patient intravenously in 1½ months. In our experience, higher doses of stabilarsan are not tolerated by the patients.

VII. *Thio-bismol*.—Total number of cases treated was 15; of these 13 gave a strongly-positive Wassermann reaction and 2 a moderately-positive reaction. Dose—10 injections of 0.2 gramme were given intramuscularly into the buttocks to each patient in 2 months. In our experience, higher doses of thio-bismol are not tolerated by the patients.

VIII. *Quino-ido-bismuth*.—Total number of cases treated was 15; of these 13 gave a strongly-positive Wassermann reaction and 2 a moderately-positive reaction. Dose—6 injections of 4 cubic centimetres were given intramuscularly to each patient in 1½ months. In our experience, higher doses of quino-ido-bismuth are not tolerated by the patients.

IX. *Bismuth-idol*.—Total number of cases treated was 10. Of these 9 gave a strongly-positive Wassermann reaction and 1 a moderately-positive reaction. Dose—8 injections of 2 cubic centimetres were given intramuscularly to each patient in 1½ months. In our experience, higher doses of bismuth-idol are not tolerated by the patients.

TABLE II

Showing the comparative value of thio-sarmine and other drugs in figures on Wassermann reaction after treatment in 240 cases of syphilis

	BEFORE TREATMENT			AFTER TREATMENT			
	Strongly positive	Moderately positive	Total number	Strongly positive	Moderately positive	Doubtful	Negative
Thio-sarmine ..	23	7	30	2	4	8	16
Sulfarsenol ..	19	11	30	11	10	7	2
Sulfarsenol and bismostab ..	7	3	10	4	5	1	nil
Novarsenobillon ..	27	3	30	10	12	4	4
Novarsenobillon a n d bismostab ..	28	2	30	10	7	8	5
Novarsenobillon a n d mercurisol ..	27	3	30	10	10	6	4
Stabilarsan ..	27	3	30	17	7	5	1
Thio-bismol ..	13	2	15	8	4	2	1
Quino-ido-bismuth ..	13	2	15	6	6	2	1
Bismuth-idol ..	9	1	10	4	3	nil	3

TABLE III

Showing the comparative value of thio-sarminc and other drugs, in percentage on the Wassermann reaction after treatment calculated from the figures in table II

	Strongly positive	Moderately positive	Doubtful	Negative
Thio-sarminc	6.6	13.3	26.6	53.3
Sulfarsenol	36.6	33.3	23.3	6.6
Sulfarsenol and bismostab ..	40.0	50.0	10.0	nil
Novarsenobillon	33.3	40.0	13.3	13.3
Novarsenobillon and bismostab ..	33.3	23.3	26.6	16.6
Novarsenobillon and mercuriosol ..	33.3	33.3	20.0	13.3
Stabilarsan	56.6	23.3	16.6	3.3
Thio-bismol	53.3	26.6	13.3	6.6
Quino-ido-bismuth	40.0	40.0	13.3	6.6
Bismuth-idol	40.0	30.0	nil	30.0

Observations

(1) It will be seen from the above that thio-sarminc is a most efficacious drug in the treatment of syphilis and its manifestations.

(2) Intolerance towards this drug is much less than with other arsenobenzene compounds.

(3) The effect on the Wassermann reaction is remarkable in the case of thio-sarminc as will be seen from tables II and III; the largest number of cases showing negative Wassermann reaction after treatment was noted in the case of thio-sarminc.

In compiling this paper we have not in any way selected cases for treatment as being likely to respond, but each case has been taken in the order of admission, irrespective of the gravity of disease or nature of symptoms. All cases have been positive in blood reaction and without exception the lesions have been gross and extensive. Side by side with thio-sarminc treatment, other cases have been undergoing treatment with other preparations. Amongst the advantages we have noted clinically are absence of reaction in cases treated with thio-sarminc. The temperature hardly ever rises, and there is practically no pain. There have been no nitritoid crises, nor anaphylactic conditions and hitherto no arsenical dermatitis. The drug may be regarded as one of the most innocuous at present in use, its lack of toxicity being most marked in comparison with its high efficacy. It appears to be, so far, most suitable both for hospital and private use. Furthermore the rapidity with which symptoms disappear compares very favourably with other preparations. Our experience in this hospital is that the ordinary Indian female patient is intolerant of novarsenobillon in doses over 0.45 gramme and it is our practice never to exceed this. The usual onset of dermatitis when it occurs is after the 4th injection, or if the dose of 0.45 gramme has been exceeded. With thio-sarminc the maximum dose has been up to 0.6 gramme without the slightest effect. It is to be remembered that the dosage of the arsenical compounds, such as novarsenobillon, neosalvarsan,

etc., has been based on the physical characteristics of the European and it is now known that the Indian female cannot tolerate a dose well-borne by her European sister. This does not, however, seem to apply in the case of thio-sarminc. We have observed no case in which the Indian female has shown intolerance even in the higher doses. It therefore appears clinically that it is of a comparatively low toxicity.

THE ANTIGENIC POWER OF ANTI-DYSENTERIC BILIVACCINE, AS DEMONSTRATED BY A SEROLOGICAL METHOD

By PROF. P. SEGUIN

Institut Pasteur, Paris

SINCE the work of Besredka has popularised the methods of oral vaccination, different methods have been sought of effecting by means of oral administration, vaccination against cholera, typhoid, paratyphoid and bacillary dysentery. Numerous controlled attempts in the course of important epidemics have led us to affirm the great preventative value of oral vaccines and especially bilivaccines prepared according to the methods of Besredka.

However, as the serum of subjects immunised by the oral method contains only exceptionally and in the smallest degree specific antibodies, it was natural that a method should be sought of checking the antigenic value of oral vaccines. It is to this task that Wats and White (1931) have recently applied themselves.

These writers, after injecting into a rabbit emulsions made from tablets of antidysenteric vaccine, have never been able to obtain in the serum of the prepared animals specific agglutinins, and they have come to the conclusion that it is impossible to find dysenteric antigen in tablets of oral vaccines.

I have repeated the experiments of Wats and White and have arrived at opposite conclusions. While giving repeated injections of concentrated emulsions of antidysenteric bilivaccine into the veins of rabbits, I have observed in the

course of a few weeks the appearance in the serum of prepared animals of a relatively high titre of antibodies agglutinating the different strains of *B. dysenteriae*. As my conclusions are obviously opposed to those of the above writers, I feel I ought to give in detail one of my experiments.

I used tablets of antidysenteric bilivaccine bearing the serial number 273; these had been prepared a year and a half ago. Each tablet contains about 80 milliards of bacilli.

B. shiga 40 milliards.

B. flexner 20 milliards.

B. strong 10 milliards.

B. hiss 10 milliards.

Three tablets (that is to say a full dose) were crushed in 10 c.cm. of physiological saline and carefully emulsified. I thus obtained an emulsion of which I injected 1 c.cm. into the vein of rabbit 69 B. Eight days afterwards I prepared in the same way a new emulsion of which I injected 2 c.cm. The following week I injected 3 c.cm. of a new emulsion. Finally, a fourth injection was made of 4 c.cm. of an emulsion which was again freshly prepared.

The rabbit had therefore received intravenously in the space of 4 weeks 10 c.cm. of emulsion corresponding to the quantity of microbes contained in three tablets of antidysenteric bilivaccine. These experiments are summarised in the following table :—

	Date	Intravenous dose	REMARKS
Rabbit 69 B 2.45 kilo- grammes.	26-11-31	1 c.cm.	The animal in good health and giving no trouble.
	3-12-31	2 c.cm.	
	9-12-31	3 c.cm.	
	16-12-31	4 c.cm.	

The animal was bled 8 days after the last injection and its serum was tested against emulsions of different strains of *B. dysenteriae*.

The emulsions intended for the experiments were made directly from cultures grown for 24 hours on gelatine.

The emulsions of bacteria were used at a titre of about 60 million per c.cm.

These experiments were carried out by the macroscopic method. The tubes for the experiment were subjected to a temperature of 37°C. for 1½ hours and were then left for half an hour at laboratory temperature. We will now proceed

to the reading of the results. These are summarised in the following table :—

Dilutions

Strains used	1/100	1/200	1/300	1/500	1/1,000
Shiga.					
French, XX	+++	+++	+++	+	—
Indian, 84	+++	+++	+++	+	—
Indian, 247	+++	+++	+++	+	—
French, 162	++	++	++	—	—
Flexner.					
No. 33.	+++	+++	+++	+	—
Indian, 45	+++	+++	++	—	—
Strong, 12	++	+	—	—	—
Hiss, 3	—	—	—	—	—

It is clear from the reading of this table that all the strains which have been made use of, except the *B. dysenteriae* of Hiss, have agglutinated in the presence of the serum of the prepared rabbit.

Shiga and Flexner strains have strongly agglutinated in a dilution of 1/300.

Note that the strains of *B. shiga* 247 and 162 and the Flexner strain have not been utilised for the preparation of tablets of *B. dysenteriae*, the emulsions of which have been injected in the rabbit.

To conclude, there is no doubt that although the degree of agglutination observed is neither as high nor as easily obtained as that which is readily observed in the case of animals injected with heated microbial emulsions freshly prepared from a strain of *B. dysenteriae*, it is nevertheless possible to make specific antibodies appear in the serum of the rabbit by using as an antigen tablets of dried microbes. It is sufficient to inject strong doses and to make an adequate number of injections.

I attribute the absence of anti-Hiss agglutinating bodies in the serum of the prepared rabbit to the fact that this microbe is the one which in the composition of the tablet is represented by the weakest dose of dried microbes.

I think I have proved that it is possible, by making use of the prescribed technique, to give evidence of the antigenic value of antidysenteric bilivaccine by the method of specific agglutination.

REFERENCE

Wats, R. C., and White, W. I. (1931). Nature of Bacterial Substance of Oral Antidysenteric Vaccine. *Indian Med. Gaz.*, Vol. LXI, p. 435.

A Mirror of Hospital Practice

A CASE OF LYMPHOCYTIC LEUKÆMIA*

By FREDRICK H. REYNOLDS, M.B., Ch.B. (Edin.)

Civil Surgeon, Loimwe, S. Shan States

K. B., A GURKHA, aged 45 years, was admitted into hospital on 23rd June, suffering from a mild attack of irregular fever. His complexion was sallow and he was

emaciated. He had had malaria on and off, and had been taking quinine and alkalies as an out-patient, but showed no improvement. His spleen and liver on admission were just palpable, his blood did not show any malarial parasites, and there were no signs of leukæmia at this stage. He did not improve, so I examined him again on third day and found that his spleen and liver were enormously enlarged. The spleen extended 5 inches below the costal margin in the mid-axillary line and 8½ inches below it in the mammary line; the

* Rearranged by the Editor.

liver was four inches below the costal margin. The blood picture was as follows:—

Total red corpuscles per cubic centimetre ..	3,200,000
Hæmoglobin ..	55 per cent.
Total white corpuscles per cubic centimetre ..	50,000
Small lymphocytes ..	90 per cent.
Large lymphocytes ..	5 "
Polymorphonuclear cells ..	2 "
Eosinophiles ..	3 "

There were a few polymorphocytes, mast cells and nucleated red cells, also poikilocytosis and granular degeneration.

The patient perspired a great deal throughout. His abdominal and thoracic veins were distended and prominent, and here and there was marked pigmentation, but no actual hæmorrhagic areas. There was no retinal, nasal or other hæmorrhage. On admission he had slight œdema of his legs and ankles, which soon passed away.

The patient suffered a great deal from dyspnoea towards the end; this cannot all be accounted for by the enlarged spleen. His cervical, axillary, and inguinal glands were enlarged on both sides of his body. They were uniform in size, but the enlargement was slight, and they were not adherent to each other or to the skin. He was treated with arsenic and adrenalin, but the treatment was of no avail, and the patient died on the eighth day after admission and 16 days after the onset of the disease.

Comments.—This case is of interest because of its sudden onset, and its very short duration. Acute lymphocytic leukaemia is usually a disease of children and young adults but this patient was 45 years old.

The blood picture showed a preponderance of the small lymphocytes which constituted 90 per cent. of the whole white cell count. The man had not suffered previously from syphilis or tuberculosis, nor was there any history of trauma, though the constant attacks of malaria may have been a predisposing cause. A post-mortem examination was not permitted and therefore further pathological findings cannot be recorded.

A CASE OF PURPURA HÆMORRHAGICA

By S. L. BHANDARI, P.C.M.S.

Assistant Surgeon in-charge Civil Hospital, Sheikhpura

On 11th April, 1932, B. D., a married girl, aged 16, was brought to the hospital from a neighbouring village with alarming symptoms of bleeding from the throat, nose, and under the skin.

Previous history.—Bleeding from throat for four days; headache 24 hours previously, hæmorrhagic spots on legs, arms and abdomen, in the mouth, and under the conjunctivæ for the last 24 hours; and bleeding from the nose for the last 24 hours.

Condition on admission.—Temperature, 101°F.; pulse, slow and feeble; anæmic and debilitated; profuse bleeding from nose and throat; hæmorrhagic spots from pin points to the size of a large pea, on legs, arms, chest, and abdomen, as well as inside mouth, on tongue, and under the conjunctiva of the right eye; but no bleeding with urine, stools, or expectoration.

Progress of the case and treatment.—

11th April.—Calcium lactate in 20 grains doses was given by mouth every 4 hours. Bleeding was less up to 12 midnight, but started again.

12th April.—8 A.M. Bleeding still considerable; clotted blood in mouth and nose; hæmorrhagic spots

had increased both in size and number. Two cubic centimetres of hæmostatic serum was given intramuscularly at once, along with 20 grains of calcium chloride in 10 cubic centimetres of water intravenously, and the following mixture was prescribed, to be taken every four hours:—

R. Olei terebinthæ rectificati minims xv.
Acidi sulphurici aromatici .. minims xxx.
Aquam chloroformi ad .. 1 ounce.

10 A.M.—Bleeding was less.

12 noon.—Bleeding was still considerable; pulse, imperceptible; pallor had increased.

Six cubic centimetres of hæmostatic serum was given intramuscularly.

5 P.M.—Bleeding stopped; pulse just returning and perceptible with difficulty.

10 P.M.—Patient asleep; pulse better.

13th April.—No more bleeding; pulse much better; hæmorrhagic spots subsiding.

The remaining days were uneventful and the patient was discharged cured on 20th April.

AN ARROW WOUND OF THE ABDOMEN

By D. N. GUPTA

Medical Officer, In-charge Sadar Hospital, Ranchi

D. M., an aborigine of Chota Nagpur, was admitted into the Sadar Hospital, Ranchi, on the evening of 25th February, 1932, with a wound in his abdomen made by an arrow which was still *in situ*. He had been hit in the morning at about 9 A.M. of the same day. The illustration shows the position of the arrow. An operation was performed and the arrow was removed; it was found to have pierced the abdominal wall and the parietal peritoneum, and to have damaged the great omentum. Recovery was uneventful and the patient was discharged cured on 11th March.



The bow and arrow is still in vogue amongst the aborigines in this part of India. From a medico-legal point of view it is important to note that these people commonly use aconite on the tip of the arrow for homicidal purposes and for big game hunting. In this case there was no such poison used.

ENCEPHALITIS LETHARGICA IN ASSAM*

By NISANATH GHOSH, M.B.
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Dibrugarh, Assam

Occurrence in Assam.—So far as the knowledge of the writer goes no case report of encephalitis lethargica has yet been published from Assam. Hence he ventures to record his observations.

In 1926 the writer happened to see in a village in the Surma Valley a comparatively young man with symptoms of paralysis agitans. This made him suspect the prevalence of encephalitis lethargica in sporadic form in Assam.

Since 1926 several suspicious cases and at least 3 undoubted cases of encephalitis lethargica have come to the notice of the writer.



Fig. 1.

Case 1.—B. C. D., Hindu, male, aged 25 years, a cultivator by occupation, was admitted in the Dibrugarh Hospital on 21st September, 1929.

Past history.—He had coryza and fever about a month prior to admission. The fever lasted for about two weeks. He was unconscious during that period. After that there was a change in his temperament. He became violent and abusive and used to spit here and there. For the last 10 days before admission he was becoming dull and listless.

Condition on admission.—He was dull, and apathetic. His face was expressionless and he lay motionless in

*Rearranged by the Editor.

bed for hours on end with his eyes closed. The patient used to pass urine and faeces into the bed and did not take food unless fed with a spoon.

Examination.—His eyes showed—ptosis, slight lateral nystagmus, unequal pupils and sluggish pupillary response to light. No sign of facial or palatal paralysis was discovered. In erect posture his body was slightly bent forwards with the arms in front kept semiflexed and rigid. All movements were slow and stiff. Athetoid movements and tremor of the fingers, tremor of the tongue and eyelids were found. Speech was indistinct. He was very slow to respond to calls and never gave intelligent answers to questions. He could not walk and when he attempted to do so there was a tendency to fall forwards. The attitude and facies were suggestive of Parkinsonism. Knee-jerks were exaggerated. Babinski's sign was markedly positive. The feet were slightly cedematous. The pulse rate was 75 per minute and the temperature, was 98.4°F. There was no well-marked rigidity at the neck. Kernig's sign was absent. Urine, normal. Lumbar puncture yielded clear fluid under normal pressure, with a few lymphocytes. The general appearance of the patient is seen in the accompanying illustration which was taken after about two weeks' stay in the hospital.

Treatment.—Besides occasional symptomatic remedies hexamine was used regularly. Hyoscine hydrobromide was used for the Parkinsonism and lessened the rigidity appreciably. He was taken away from the hospital after about a month's treatment on 24th October, with the lethargy and rigidity somewhat improved.



Fig. 2.

Case 2.—The patient, named S., Hindu, female, a coal-mine coolie aged 30 years, was admitted on 23rd January, 1931, and was discharged on 16th February, 1931.

Her complaints were.—Inability to move about properly and inability to work for the past five months, after an attack of fever lasting for one week during which she remained unconscious for three to four days.

Past history, habits, etc.—She came to Assam in her babyhood and has never been outside the province since

then. She is accustomed to smoke tobacco, to take tea and occasionally alcohol. She has had occasional attacks of fever, each of short duration, in the last two years—the last attack ending in the present trouble.

Condition on admission.—Her attitude, facies and gait were typically Parkinsonian in character. Rigidity of the body and limbs was very marked. Tremor was present but was not exactly of the 'pill-rolling' type and it used to disappear on sleep. All movements were sluggish and stiff. Speech was slow and indistinct. Knee-jerks were very brisk. Babinski's sign was doubtful. The right eye had a squint. The eyelids were tremulous on closure and the tongue was tremulous on protrusion. The patient was apyretic and could manage to move about unaided. The spleen was enlarged 3 inches below the costal arch. Accompanying illustrations of the patient in two positions show many of the above-mentioned features.



Fig. 2a.

Treatment.—Hyoscine and hexamine were mainly used. Very little improvement was noticed on discharge.

Case 3.—The patient, named B., Hindu, male, aged 24 years, was admitted on 24th March, 1932, and on 1st April, 1932, he was removed by his relatives from the hospital, against medical advice.

Complaints.—Inability to walk about and extreme listlessness and idiotic behaviour for the past fortnight.

Past history, illness, etc.—He was said to be literate enough to sign his name in English prior to his illness. About three weeks before admission he had fever lasting for one week. After the fever the present symptoms were noticed.

Condition on admission and during stay in hospital.—His attitude and facies were suggestive of Parkinsonism. He was unable to walk unaided, so his gait could not be tested. On standing up he had a tendency to fall towards the right side. There was ataxia and slight drooping of the right upper eyelid and also squint in the same eye. He was dull and listless but sometimes kept wide awake all night. He lost his speech and made an ineffectual attempt to write, resulting in

scribbling only. Urine and faeces were usually passed into the bed. Knee-jerks were normal. Babinski's sign was absent. There was slight rise of temperature at times. Lumbar puncture was not done.

Treatment.—The same as in case 2. Though the patient stayed for a short time in the hospital there were definite signs of improvement at the time of discharge. He was more wakeful than before, was able



Fig. 3.

to stand up unaided and his squint had disappeared (see accompanying illustration). All these improvements were probably due to a natural process and not to the treatment he had in these few days.

The writer is grateful to Lieut.-Col. Colin McIver, M.D., D.T.M. & H., I.M.S., Superintendent, B. W. Medical School for his encouragement and valuable help.

LEECH BITE OF LABIUM MAJUS*

By C. S. P. HAMILTON, M.R.C.S., L.R.C.P.

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THE following case is of interest in that the symptoms might have led to a diagnosis of uterine hæmorrhage being made.

I was called to see a lady who was suffering from hæmorrhage.

* Rearranged by the Editor.

Her last period was two weeks previous to this hæmorrhage, and as far as she could say was perfectly normal. She awakened on the morning in question feeling very fit; however, she became alarmed on seeing a patch of recent blood in the bed, and naturally thought she had uterine hæmorrhage. She did not complain of any local pain, and funnily enough not even of local irritation (which is generally marked in leech bites).

The patient sent for me as the hæmorrhage became more severe, but just before my arrival she got out of bed and trod on 'something slimy', which proved to be a large leech.

On examination a leech-bite wound, which was bleeding freely, was found on the right labium majus.

No other source of hæmorrhage was discovered, and there was no further bleeding.

Special Articles

LEPROSY RELIEF IN INDIA

A REVIEW OF THE PRESENT SITUATION, AND A SUGGESTED POLICY FOR PROVINCIAL AND LOCAL AUTHORITIES.

By E. MUIR, M.D., F.R.C.S. (Edin.)

and

J. LOWE, M.D., Ch.D.

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The gravity of the problem

THE 1921 census gives 102,513 as the number of lepers in India, but mentions that this is short of the real number, as only conspicuous sufferers from this disease were likely to be enumerated by the untrained people who gathered the statistics. Recently, an estimate was made by the sanitation staff of a certain town in India that there were only six lepers in a certain ward of the town. Immediately after, a second survey made by skilled workers showed that there were at least 144 lepers (24 times the original figure) in that ward, and in all probability even more. It is not suggested that the 1921 census figure should be multiplied by 24 in order to arrive at the number of lepers, but we are safe in calculating that there are from one half to one million lepers in India.

Leprosy is not a very fatal disease. Compared with malaria, tuberculosis and cholera there are comparatively few deaths. But after all the death roll is not the only criterion of the suffering caused by a malady. Leprosy probably accounts for more mental, if not physical, suffering than any other disease in the country. To many lepers the prospect of speedy death instead of long years of suffering would come as a welcome relief.

While in some parts of India leprosy is decreasing, there seems to be no doubt that in other parts improved communications by rail and road, and the opening up of highly endemic areas hitherto isolated from their surroundings, are leading to marked increase and dissemination of the disease.

Recent surveys have brought to light the important part which industrial concerns play in the spreading of leprosy infection. The workers in industrial areas are drawn from different parts of the country and from different classes. The various human elements discard their customary class rules to a large extent when they leave home; they tend to mix

promiscuously, often in insanitary or crowded surroundings; and thus we have ideal conditions for the spread of a chronic infection like leprosy. This state of affairs has been brought out by our survey figures which show an incidence of at least one per cent. in almost all industrial areas, and this number rises to three per cent., or even higher, in some places. A very heavy responsibility devolves upon those who are in charge of sanitary measures in these areas.

B. E. L. R. A. (Indian Council) and its policy

The Viceroy appealed in 1924 for funds to form a branch of the British Empire Leprosy Relief Association in India. A sum of over 20 lakhs of rupees was subscribed and the question arose as to the best method of using this money. Since the discovery of the bacillus of leprosy by Hansen in 1872, the accepted method of dealing with the disease has been through segregation in leper asylums. Judging from the expense involved in founding and running these institutions it would not have been possible to arrange for the segregation of more than one or two thousand lepers with the amount available. Moreover the majority of lepers who migrate to such institutions have in the past been those who have reached the last stage of the disease in which the infection is dying out, and who have already spread the infection to their relations and neighbours.

New line of campaign.—It was decided therefore that a new line of campaign was necessary. Research had recently shown two things:—(1) that leprosy can be diagnosed with ease in almost every case at a stage when the patient has not begun to be infectious and a danger to others, and (2) that at this stage most cases treated efficiently and for a long enough time recover.

It is easily understood therefore that a scheme which aims at diagnosing and treating all early cases and organising prevention is likely to be much more effective in controlling leprosy than one which can only hope to segregate in asylums some two or three thousand out of the half to one million lepers of India.

Accordingly the policy adopted by the Indian Council of the British Empire Leprosy Relief Association has been:—(1) the diagnosis and treatment of all but especially early cases, and

(2) prevention. In order to secure this, the following programme is being followed out :—

1. *Training of doctors.*—Till recently leprosy has not been considered a remediable disease. It has therefore not been studied by the medical profession, and many doctors are unable to diagnose any but the most obvious cases. If early cases are to be diagnosed and effective treatment is to be adopted, it is necessary for all doctors to become acquainted with the disease especially in its early stages and to know how to treat it. Instruction in leprosy is now given to the students of many medical schools. Short courses of instruction have also been held in Calcutta, four every year and each lasting two weeks, at which doctors from the various provinces and states of India have received the necessary training. Many of those who have attended these courses have trained other doctors in their own provinces, and in this way, as well as by means of suitable literature, it is hoped that within a few years most of the doctors in India will be as conversant with leprosy as they are with malaria.

2. *Survey of incidence of leprosy.*—Obviously, if effective means are to be taken to deal with leprosy, we must know in what parts of India the disease is most common and among what classes of the community it is most rife. Also, if a higher incidence is found in certain areas and among certain classes of people, the reason for this must be ascertained. The census taken in the first year of each decade enumerates only the more obvious cases and, as has been mentioned above, the real incidence is probably from 5 to 10 times as great.

Obviously, it is impossible to make an accurate survey of all India. It has been found that a party of five skilled workers take one month to survey a thana with a population of 40,000 people. It would therefore take 70 such parties, working for 10 years, to survey all India. What was done was to appoint a party, which visited the various provinces and states in turn, making demonstration surveys in an area of each province which had been ascertained by the 1921 census to be highly leprosy. The effect of this sample survey was to induce provinces and states to appoint similar survey parties of their own to carry on work along similar lines.

The method of carrying out a survey is as follows :—

A treatment centre is started in what has been shown to be a highly endemic area. Infectious cases are followed up to their villages and contacts are examined for early signs of the disease. The villagers are shown by practical demonstration, posters and magic lantern slides what are the early signs of leprosy, how the disease is conveyed from one person to another and also that good results can be had from treatment. In this way the good-will and confidence of the people are won, and patients, instead of trying to hide their disease,

come forward in the hope of being cured. It is possible to carry out a much more thorough census by the propaganda-treatment-survey method than could be done otherwise.

3. *Propaganda.*—After all, the most important factor in stamping out leprosy is isolation of infectious cases, and this can only be done as the result of propaganda and gradually educating the community as to where the real danger lies. The Association has prepared and distributes literature both for doctors and for the lay public. Among the latter an illustrated booklet entitled 'What the Public should know about Leprosy' has been translated into eleven Indian vernaculars, and sets of lantern slides, along with an explanatory booklet, can be obtained. A series of five leaflets has been prepared for distribution and has been translated into several vernaculars. *Leprosy in India*, a journal which acts as a record of progress of anti-leprosy work in India, with notes on methods used in other countries, is published quarterly.

4. *Research.*—Although the last activity of the Association to be mentioned is research, it is not the least item, but the most important of all. It was as the result of research that the Association was begun, and it is on its findings that the above programme has been founded. Much has still to be found out, for leprosy is a difficult disease to understand. Unlike the sister disease, tuberculosis, it is doubtful if its causal germ has yet been grown outside the human body; and the mode of infection and spread in the body, though worked out to a certain extent, still remain mysterious. Then much has yet to be done to improve the treatment of leprosy, and this can only be done through careful practical study by experts.

Provincial branches.—Most of the provinces and some of the states have branches of their own and a certain proportion of the funds of B. E. L. R. A. is set apart to be distributed to these branches. As examples of the work being done in various provinces by the co-operation of the provincial branches of the B. E. L. R. A. and the local governments, we may quote the following :—

Bengal.—Here the leprosy work of the province is organised by the Bengal branch of the B. E. L. R. A. with the aid of grants from government, municipal authorities, local boards, etc. There is a leprosy propaganda officer for Bengal who has visited nearly all the districts, organising courses of instruction for doctors, carrying on propaganda work, and as occasion arises doing brief surveys and starting clinics.

In addition there is a survey party of one chief and three assistant doctors who have thoroughly surveyed some of the areas of Bengal in which leprosy is most common, doing propaganda work and establishing clinics, which after the survey are then carried on by local doctors under district authorities and industrial concerns.

An interesting feature of the Bengal work has been the survey of industrial areas, jute mills, mines and tea gardens.

In Bengal there are over seventy leprosy clinics started by the B. E. L. R. A. workers and being carried on by doctors appointed and supported by local authorities.

The Bengal branch has a small income which has been sufficient to support only one good leprosy officer; but he, by ability and keenness, has been able to enlist the co-operation and financial support of government and local authorities, so that the work has developed widely. If the funds of the B. E. L. R. A. had been used to finance clinics, the result would have been only two or three clinics and not the present large number.

Madras.—The survey party of the Indian Council of the B. E. L. R. A. has visited this presidency on two occasions and as a result the Madras Government, in consultation with the senior writer, have drawn up a scheme of anti-leprosy work in the presidency. The presidency has been divided into six areas for each of which has been appointed a special leprosy officer to carry on propaganda and survey work, create treatment centres attached to suitable medical institutions, train doctors, and generally organise and co-ordinate leprosy work. By co-operation with the public health department it is hoped to complete a more or less accurate register of all leprosy cases detected. This it is planned to check by quinquennial surveys by public health authorities.

Attempts have been made in Madras to co-ordinate the work of leper asylums and leprosy clinics.

There are in existence about 80 clinics financed by government and local authorities. The funds of the Madras branch of the B. E. L. R. A. are handed over to the government to help to pay for the leprosy staff.

Madras being more developed than many other parts of India the government are able to consider the organisation of a definite scheme of widespread leprosy work. The progress of this work will be watched with interest.

Bihar and Orissa.—This branch distributes part of its income in grants to clinics and hospitals treating leprosy. The government had a leprosy officer and a survey party, and it was reported in 1931 that there were 36 clinics. In addition there was a whole-time leprosy officer in the Puri district, and an annual grant from the Bettiah Raj estate paid for two whole-time leprosy officers in the Champaran district.

The government have as a measure of economy abolished the post of leprosy expert and the survey party, so that in spite of a considerable amount of money being available from the B. E. L. R. A. and other sources, the development of anti-leprosy work in Bihar and Orissa is likely to be handicapped.

Central Provinces.—After a visit of the B. E. L. R. A. (Indian Council) survey party in 1928,

a leprosy specialist was appointed and a survey party of four doctors was formed. Systematic survey work was carried on and 32 centres were established. Sixteen of these were placed under the charge of special assistant medical officers working under the public health department, the remainder being run by local dispensary doctors. The special assistant medical officers run leprosy treatment centres and subcentres; they carry on steady propaganda and survey work in villages and combine with their leprosy work a considerable amount of general public health and epidemic work. This work has steadily progressed. The clinics run by the local assistant medical officers in connection with the existing dispensaries and hospitals have not been nearly so successful, and experience has shown that leprosy work is best done in the Central Provinces under the public health department by special officers who make leprosy work one of the main activities in a campaign for rural public health.

The work in the Central Provinces is an interesting experiment in the use of methods of organisation rather different from those used elsewhere. Every year survey work is done and an increase in the number of clinics and patients is recorded and the results are reported as being very encouraging.

Reports of work done in other provinces are published in the annual report of the B. E. L. R. A. (Indian Council).

The results of this work

(1) *Survey work.*—The survey has brought out many useful and interesting facts among the chief of which are these:—

- (a) Leprosy is most prevalent among semi-aboriginal tribes who have left their aboriginal seclusion but have not yet adopted the modern sanitary measures common among more civilised people.
- (b) Leprosy frequently enters better class families through these semi-aboriginals when they are employed by such families as servants.
- (c) A single highly-infectious case may often infect not only a village, but indirectly a group of villages.
- (d) The commonest form of leprosy found is the 'neural' form showing anæsthetic macules or acroteric lesions. These cases are presumably non-infectious since no bacilli can usually be found in them. Some of these cases undoubtedly progress later to the cutaneous form which is infectious, but some of them do not. Some cases, exactly what proportion it is difficult to say, undergo spontaneous arrest. At any one time two or three 'neural' cases are found to each 'cutaneous' case.

- (e) The finding of large numbers of slight cases in a village indicates one or two

things. Either the disease has been newly introduced and is spreading rapidly; or the village has long been infected but, since the people have a high degree of resistance, the disease takes a mild form.

- (f) There is generally a fairly obvious predisposing cause. Often there is some other disease, such as syphilis, malaria, hookworm disease, or filariasis. Sometimes it is the diet of the people. At other times it is the climate or geological conditions resulting in occasional famine or chronic under-feeding. These causes vary in various districts, in different villages, and in individuals.

(2) *Treatment and prevention.*—One of the results of this campaign is the general recognition that the leprosy problem, though a difficult one, is not incapable of solution. Large numbers of special leprosy clinics have been started, and in many general dispensaries provision is now made for the separate treatment of leprosy on certain days. A recent questionnaire sent round at the request of the League of Nations shows that at the end of the last year there were 59 residential institutions for leprosy in India with a total of 9,634 inmates, most of whom are under treatment; also that there were 213 out-patient clinics, either special or general, in which leprosy was treated. All this shows that it is now generally recognised that leprosy treatment is worth while. But unfortunately the great majority of patients lack perseverance, or are unwilling to take the time and trouble required for complete recovery. Also ignorance, superstition, unhealthy surroundings, and adverse economic conditions stand in the way of their improvement.

It is however being realised more and more that treatment alone is never likely to stamp out leprosy in India. Efforts to get patients to attend regularly for treatment must not be diminished, but the chief function of a leprosy clinic should be prevention. It is easier to prevent a dozen cases of leprosy than to cure one.

Prevention can only be carried out by following up the patient from the dispensary and visiting him in his own home. As far as possible every clinic should make arrangements for this follow-up of patients, and specially trained workers may be necessary to do it efficiently. General propaganda, such as may be given in the clinic itself, is not likely to carry much weight. Leprosy is primarily a village disease, and it is not the single person but the community that forms the village unit. The whole village must be instructed and persuaded, otherwise there will be no permanent result. Moreover the outlook and interests of villagers are narrow; they are not interested in abstract ideas and general statements. It is necessary for the leprosy worker to visit the

village, follow up the infectious case, gain the confidence of the inhabitants and enquire into the history of the origin and spread of the disease in that particular village. From this information he should prepare his special propaganda, explaining not in general but in particular terms how leprosy can be prevented.

Leprosy can only be controlled by limiting the opportunity of spreading infection. We do not know the exact mode of spread of leprosy, but certain important facts are now generally accepted. Leprosy is spread by contact of infective cases with healthy people. The more intimate the contact and the greater the period of contact, the greater is the danger. Children and young people are much more susceptible to leprosy than adults. Prevention must aim at preventing this contact specially with young children. Isolation of all infective lepers in institutions is impracticable in India, but much might be done to carry out isolation in villages and in homes. The type of contact which is most dangerous is the type which is commonly seen in joint-family houses at night, infective lepers sleeping together with healthy members of the family in a small crowded room. This should if possible be prevented. In some villages it may be possible to have huts put up outside the village where infective lepers should live and sleep. They can go about and work if possible during the day, but they must sleep in separate quarters at night. The same applies to the homes of lepers. A separate room or a hut outside the joint-family house, for the infectious case to live and sleep in, is very essential. Even now this is sometimes provided by the families of lepers, but only when the patient has become deformed, unsightly and ulcerated. This is too late. Many patients have been infective for years before they reach this state, and in fact the deformities and ulcerations are often a sign that the infective stage is drawing to a close. The village or home isolation must be carried out much earlier and much more efficiently. Too often one sees infective lepers living in a separate hut, but attended by the children of the family. Thus the home isolation is rendered worse than useless, for children are much more susceptible to leprosy than adults. In home and village isolation, arrangements must be made for separate eating and drinking utensils, as well as for separate sleeping accommodation, and the importance of protecting children from infection must be realised.

The great predisposing causes of leprosy in India are the bad social and hygienic conditions of the people. Bad housing, bad diet and debilitating diseases render people susceptible to leprosy and provide the conditions under which leprosy spreads. Therefore all measures which tend to improve social and hygienic conditions and to help people to love a healthy life will also tend to bring about a diminution in leprosy. Leprosy propaganda should therefore merge into the wider sphere of general public health work.

The following figures are extracted from the official report for 1930. The figures for that year are chosen for quotation as it is for that year that they are published in a form which lends itself to this analysis. In that year too, the Health Boards Enactment had placed all estates, European and Asiatic, under the charge of a medical officer.

drainage of this sort, with neither oiling nor any other auxiliary has been found in this practice sufficient to control *A. ludlowi*.

Anopheles umbrosus has been dealt with entirely by concentrating all water, and maintaining it open to the sunlight in clean-cut channels or containers free from all surface vegetation. The application of oil has

TABLE I
Hospital and death rates for 1930

		Population	Hospital admissions	Hospital rate per mille	Deaths	Death rate per mille
All estates of F. M. S. ..	{ All causes	280,721	84,581	301.3	5,784	20.6
	{ Malaria		25,744	91.7	782	2.8
Selangor estates ..	{ All causes	104,474	30,522	292.1	2,155	20.6
	{ Malaria		8,044	76.9	205	1.9
Estates in Klang and K. Lgt. districts.	{ All causes	41,505	11,232	270.6	824	19.6
	{ Malaria		2,725	65.3	45	1.1
Similar figures for the estates under the control of this practice throughout that year are:—						
	{ All causes	18,398	4,367	237.3	341	18.5
	{ Malaria		597 *	32.4	10	0.5

* Comprising: 387 benign tertian, 131 sub-tertian, 17 quartan, 29 undefined, and 33 carriers without symptoms.

The problem of malaria in Malaya has been noteworthy for its high epidemicity especially when the work of agricultural expansion was taking place. As the country grew so did the serious aspect of malarial sickness and death. All methods of control by clinical treatment seemed of equal success inasmuch as they had no effect for the better. At this juncture, when the whole commercial foundation of the country was at stake, the advent of anti-larval methods took place.

The area to be dealt with being widespread agricultural country, what has become known as species sanitation was adopted, so that the anti-larval attack was directed only against those mosquitoes which were the proven vectors in the district. These anti-larval measures varied therefore with the species found and their natural predilections for certain environments and conditions, and with the topography of the locality.

The malaria vectors implicated were *Anopheles ludlowi*, *Anopheles umbrosus* and *Anopheles maculatus*. While admitting the possibility of other species being upon occasion capable of carrying infection, the writer's experience is that, in Malaya, in the absence of these three species, epidemic malaria does not occur.

The earlier work in this practice has been described elsewhere (Watson, 1921), and the methods there given in detail have been followed with but little alteration since that time. In the writer's experience success still invariably follows the proper application of anti-larval methods for the control of malaria, but, except in so far as a record of success of any particular method is of itself evidence in its favour, these notes are not intended as a defence of any one method as opposed to another. They are simply a record of experience of the writer in the field of malaria control.

Anopheles ludlowi, the brackish water breeder is dealt with by bunding and the provision of good drainage through tide gates. This mosquito is, of course, typically found on the coast, but with faulty and leaking bunds and gates, or in their absence, it is surprising how far inland it may be found on flat land. Efficient

proved, not only unnecessary, but ineffective in controlling this species.

Measures against *Anopheles maculatus* have also depended primarily upon drainage, that is, on the concentration of all water in well-defined channels. These have been either of sub-soil type, or open concrete channelling or open earth drains. Only the last have been oiled.

Drainage, it will be noted, is the basis and *sine qua non* of all the anti-larval methods employed, and the progress of these measures towards some degree of perfection the writer hopes to show below.

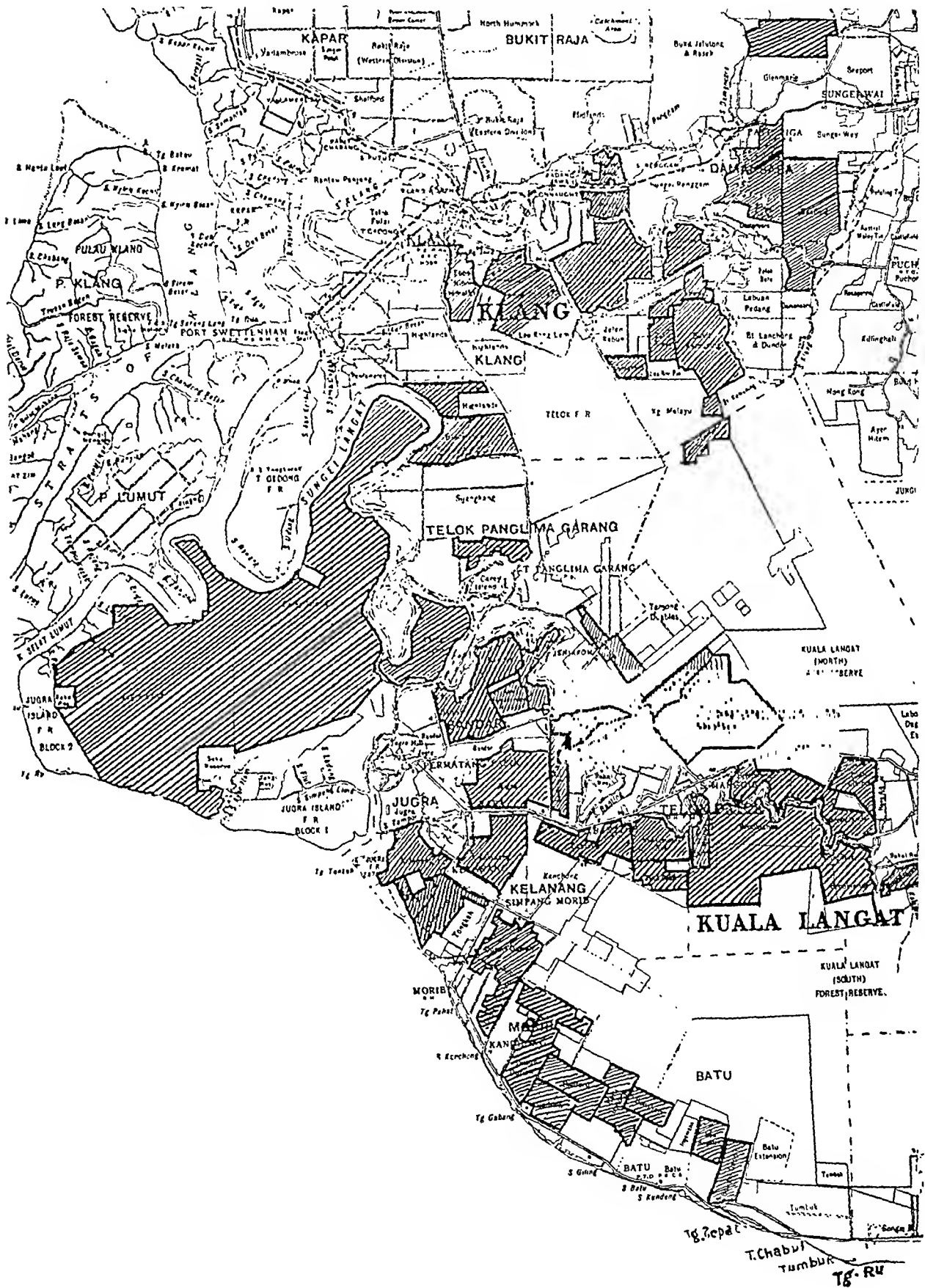
Scientifically, anti-larval methods seem logical and sound in principle. It may be claimed, however, by critics that no controls are available. It is admitted that controls for each little peculiarity are difficult to obtain, but in some cases there are such controls which are considered good enough for the purpose. Moreover, controls due to the removal of anti-larval methods and the re-introduction of these methods in the same locality are available.

The whole subject of anti-larval control in this country has been tried and tested *pari passu* with the progress of knowledge of the subject, until a stage has been reached which, if not of perfection, is at least one of a high degree of success. It is the writer's opinion that, if these methods were pushed to the limit, no economic factor intervening, practical perfection would obtain. To support this contention examples will be given on separate entities and of the factors which counteract actual perfection being obtained. The latter factors will be explained and enumerated first so that a better criticism of the estate results can be made. These factors fall chiefly under the following heads—(i) topography, (ii) the human element, (iii) insufficiency of quarantine or of control over the population (estate immigration and visiting), and (iv) the economic factor.

The topographical factor is probably the most insistent counteracting influence. This is best appreciated by a study of the map of the locality. Here we see anti-larval control on small estates more often than not

MAP I

Map of the district. The estates of this practice are shaded and show the large periphery liable to invasion by mosquitoes and malaria.



hedged round by other agricultural land which has no mosquito control in any form. These alien areas are often within mosquito striking distance of the habitations of the controlled labour forces, although to avoid this should be the first step of an anti-malarial policy. This is made apparent when no long view has been taken and temporising measures have prevailed. With foresight and courage most of the heavy initial expenditures on attacks on Nature's strongholds would actually have paid in a short time, but where, for example, the control area round the habitations is insufficient, on account of unwillingness to face initial expenditure, a definite counteracting factor to perfect anti-larval control is present.

Even when more than half mile from housing, these areas still form a source of infection to night visitors. Furthermore, work on an estate often starts in the half light of the morning and workers may be infected while operating near these boundaries. With most estates there is a relatively large boundary line thus adjacent to a non-controlled and endemic area.

The human element in all ventures is apt to fail at times and no less so in any method of malaria control. The carrying out of the various procedures must be definite and exact, and here alone error may occur. Constant care must be as permanent as the structures used, and work put off till to-morrow will surely exact its toll. As the effects of good anti-malarial work can only be seen in a negative light there is a great temptation at times for a worker to allow himself a certain amount of easing up. This negative character of the evidence of the best work in malaria control often, too, tempts the onlooker to consider as the most superfluous, the worker with the greater achievement to his credit.

The total number of cases of malaria treated on Carey Island during the past five years has been 159, or 0.6 per cent. per annum of a population of five thousand persons.

Of these 52 were admitted within 10 days of arrival on the estate, 27 were admitted between 10 and 20 days, 23 were admitted between 20 and 30 days.

Of the remaining cases 17 gave a history of fever elsewhere during the previous six months and 9 during the previous one year. Of the remaining 31 cases 14 had the infection traced to the uncontrolled Sakai reserves on the island. Only 17 cases or 0.6 per cent. per annum remain unaccounted for. These include all parasite carriers who had shown no clinical symptoms, but whose blood had been examined as a routine measure.

If, in order to satisfy the most critical, we accept as imported only those cases detected within ten days of arrival, we have one-third of the cases imported. As communication with Carey Island is by private ferry and costs money, it is clear that this proportion must be very much higher on healthy estates completely surrounded by easily-accessible infected country.

The anti-malarial measures adopted on Carey Island consist of deep drainage and well-constructed and well-supervised tide gates, and the siting of all housing over half a mile from uncontrolled areas. The potential vectors are *A. ludlowi*, and, to a lesser extent, *A. umbrosus*. No oiling has been done on Carey Island, which has over 17,000 acres under cultivation, and the malaria incidence since 1921 has been under one per cent. per annum.

This work on Carey Island was conducted from the opening up of the estate, and has prevented the introduction of epidemic malaria to any important extent to the foreign labour brought to work the estate.

TABLE II
Malaria rates on Carey Island estate

Year	Population	Malaria cases	† Malaria rate per mille	Malaria deaths	* Malaria death rate per mille
1921	4,400	60	13	4	0.9
1922	4,321	26	6	2	0.4
1923	4,424	20	4	1	0.2
1924	4,573	16	3	1	0.2
1925	4,844	15	3	nil	nil
1926	5,223	24	4	1	0.2
1927	5,651	28	5	nil	nil
1928	5,197	36	7	1	0.2
1929	5,838	38	7	2	0.3
1930	5,410	32	6	1	0.2
1931	4,989	25	5	nil	nil

* All cases having parasites in the blood are included, whatever the specific cause of death.

† Includes imported cases. No correction for these cases is made in any of the tables given.

There have been times in the history of every estate when labourers were required in increasing numbers. This immigration, especially in times of exigency, had no effective control. Here a leakage took place and there appeared in the labour force cases of malaria whose infection had been contracted on the unhealthy estates from which they came. No control over the population has ever been effective as regards their habits of wandering from one area to another, whether for one night or for extended periods of time.

The map of the area of this practice clearly indicates the vast opportunities provided for these imported cases, much of it being small detached areas completely surrounded by uncontrolled country where anopheline vectors, high spleen and malaria rates, of anything from 30 per cent. to 100 per cent., abound.

As an example of the extent to which such imported cases can effect the incidence rate in areas under full control the figures of Carey Island estate, where some form of quarantine is possible, are of value.

Several controls are available for the work done. Carey Island is identical in character to, and is situated at the mouth of the same river as, Port Swettenham, and the malaria history of that port is well known to have been so bad that, after it was built, the Government ordered it to be abandoned.

Two areas of uncontrolled Sakai (aboriginal) reserves on the island itself, with their numerous *A. ludlowi* and *A. umbrosus*, and their high malaria endemicity, are further controls for the work on the cultivated portion of the island.

There have too been incidents in the history of the estate which themselves serve as controls. Some years ago 300 coolies left the island and went to an estate in Malacca. Some months later 200 returned, all heavily infected with malaria. No isolation of these reservoirs was attempted yet no infection was passed from them to any other cooly.

A contrast to this was provided in 1920, when 19 cases of malaria occurred in one division. This outbreak was

traced to a disused well which had been allowed to become overgrown with weeds and in which *A. umbrosus* was found. In 1928 five cases of malaria occurred in coolies who had not left their division. A survey revealed a few *A. ludlowi* in the drain. Further investigation showed a slight undermining of the tide gate controlling the area, which permitted the ingress of salt water.

Over the area of the practice where malaria was already hyper-endemic among the labour forces before work was started the figures of past years are incomplete in some respects, but with every person known to have had malaria more than once in the year, progress is fairly shown by the annual death rates. In the past all statistics were noted for workers only and the death rates of these, from all causes, fell from 67 per mille in 1908 to 8.5 per mille in 1930.

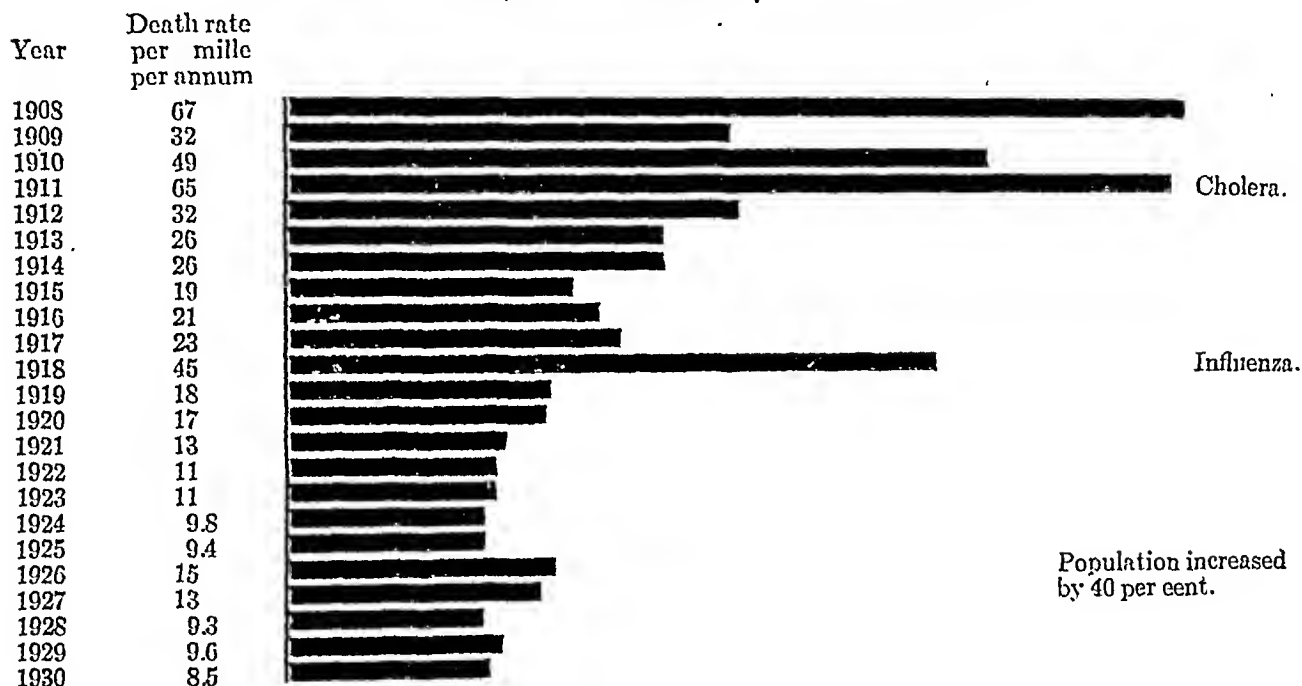
surveys using thick blood films, the technique followed being that described by Green (1931).

These have been as yet completed only for a relatively small area. In the case of the estate which produces the highest malaria rate, viz, 10.0 per cent. per annum, the parasite rate was 11.3 per cent. When a sufficient length of time for proper observation has elapsed the results of treatment with plasmoquine on these carriers will be reported.

Estate P. in 1930 gave an incidence rate of malaria of 5.3 per cent. of the population per annum. A parasite survey, by the officers of the Institute for Medical Research, of 415 persons gave 32 positive or 7.7 per cent. The hospital books of this estate show that at one time a 'burial gang' drew, almost constantly, overtime pay for their work, and the death rate was for years around

CHART I

Death rates from all causes of estate workers



As the incidence of malaria fell below 100 per cent. this has been recorded separately for the whole population, and over an area of some 130 square miles, of what was at one time as malarious a part as anywhere

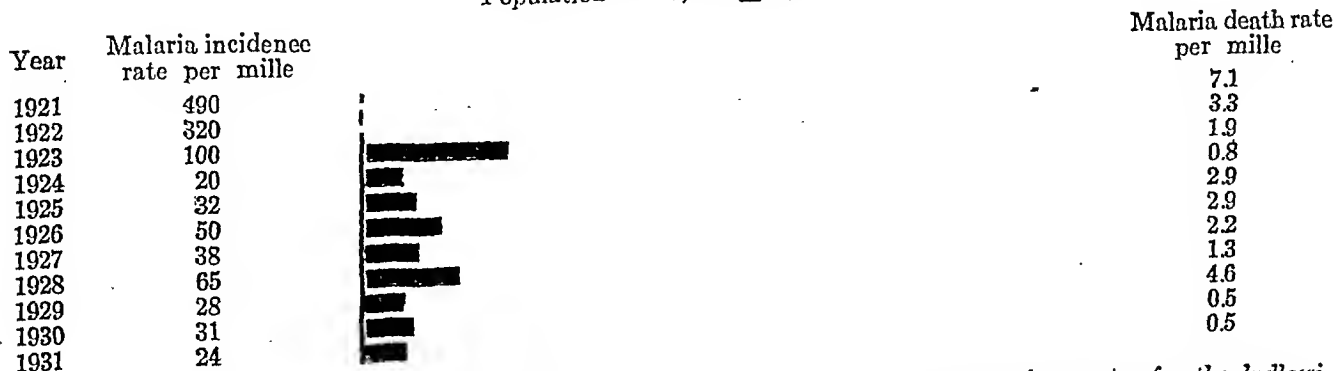
300 per mille per annum. The malaria incidence rate in 1931 was 1.2 per cent.

Chart II shows the malaria incidence and death rates for the entire area of this practice since 1921, while the

CHART II

Rates per mille over the whole practice

Population = 17,000 \pm 4,000.



in the world, the malaria incidence for 1931 was 2.4 per cent.

Now that an incidence rate has been obtained which is no greater than that which might well be caused entirely by imported cases, attention is being directed to the parasite rate as obtained by complete blood

three following charts show these rates for the *ludlowi*, *umbrosus* and *maculatus* areas, respectively. Since these areas overlap they have been divided so that the area described as *umbrosus* is composed of those estates where no other vector is found. Where *A. umbrosus* is found in addition to either of the other vectors the estate

is included in the *ludlowi* or *maculatus* area as the case may be. It is this duplication of species with opposed preferences as to breeding conditions which makes this area so much more difficult to control than those parts where only one vector has to be considered.

In these charts are included in each year all estates, whether under our control throughout the year or only for part of the year.

In the matter of effectiveness and of costs even the old subsoil drainage on this estate more than proved its worth over the fourteen years it remained, as reported by the writer (1932).

In 1926, however, the old piping was replaced. The year 1925 had been a dry one and the roots of the nearby trees had sought out the water in the pipes, which they had partially choked in some places, although this

CHART III

Rates per mille over the 'ludlowi' area

Population = 5,000 \pm 600.

Year	Malaria incidence rate per mille	Malaria death rate per mille
1921	13	0.9
1922	6	0.4
1923	4	0.2
1924	3	0.2
1925	3	nil
1926	4	0.2
1927	5	nil
1928	7	0.2
1929	7	0.3
1930	6	0.2
1931	5	nil

CHART IV

Rates per mille over the 'umbrosus' area

Population = 10,000 \pm 8,000.

Year	Malaria incidence rate per mille	Malaria death rate per mille
1921	288	10.7
1922	72	3.0
1923	57	3.6
1924	11	0.8
1925	22	2.4
1926	63	7.1
1927	40	2.5
1928	29	0.6
1929	29	0.5
1930	6	nil
1931	7	nil

CHART V

Rates per mille over the 'maculatus' area

Population = 4,000 \pm 2,000.

Year	Malaria incidence rate per mille	Malaria death rate per mille
1921	613	15.9
1922	469	7.6
1923	104	4.4
1924	23	2.0
1925	104	5.3
1926	137	6.6
1927	115	4.9
1928	177	3.6
1929	46	0.6
1930	96	1.7
1931	73	2.8

In combating *A. maculatus* two main methods are employed, viz, oiling and subsoil drainage. Shade and other methods are on no estate solely depended upon although they play their part.

Chart VI shows the malaria incidence on estate S. F. which has been subsoil-drained against *A. maculatus*. The pioneer work on this estate is described in full by Watson (1921, chapter XII), but the system as it exists to-day has been considerably modified as a result of the experience gained since that time, both on this estate and elsewhere.

did not become apparent until the excessive rainfall of 1926 when the narrowed pipes were unable to cope with the great amount of water during the floods of that year. Water seeped to the surface and was unfortunately oiled. The result of this oiling was that after the choked pipes had been repaired the oily silt prevented the water reaching, not only the newly-laid pipes but also the unbroken lines. It was therefore decided to relay the entire system. In relaying them the pipes were laid deeper and they are now five feet deep at least, and are laid in loops along the hillfoots

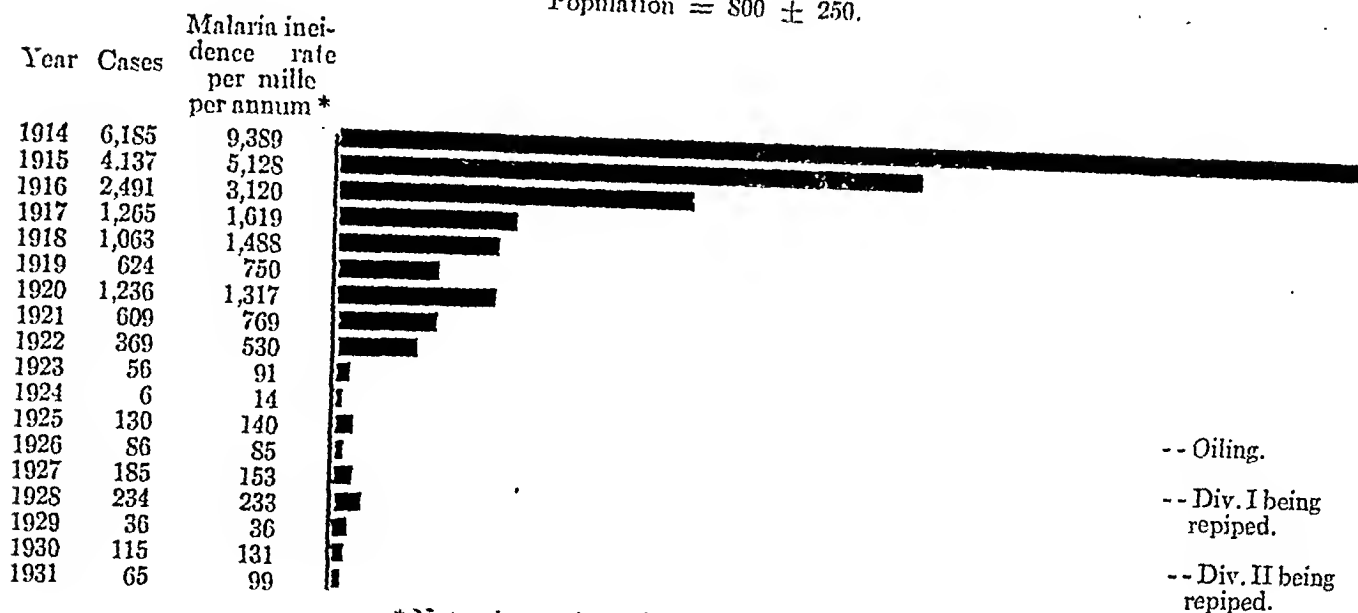
to discharge into open drains on the flatter part of the ravines. These drains are 22 feet wide at top and 2 feet at bottom which is laid with concrete channeling.

more evident that a malariologist is not merely a physician or an entomologist or a civil engineer, but something of all three.

CHART VI

Rate per mille on subsoil-drained area

Population = 800 \pm 250.



* Note change in scale of graph.

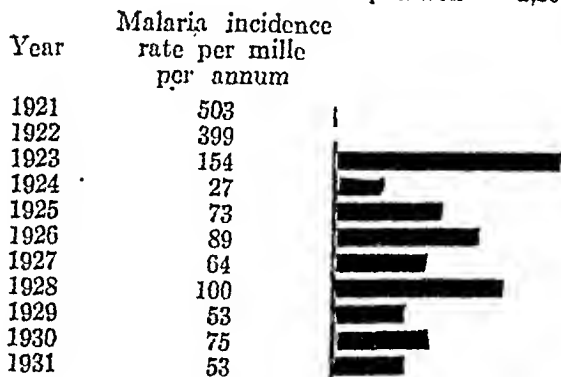
The earth sides of the drains are laid with turf and they have stood up excellently to the tremendous scour, even on Seafield estate. Only at their termination have they required repair and there the heavy

Chart VII shows the figures for these estates where oiling was considered the method of choice. The only method now used of applying the oil is by spraying from a knapsack sprayer by cooly labour.

CHART VII

Rate per mille on oiled area

Population = 2,200 \pm 300.



concrete inverts have been carried 40 to 50 feet by the scour.

Pipes are still upon occasion choked by roots. No difficulty is experienced in keeping pace with the repairs as oil is now never used over a seepage. Paris green, 5 per cent. in smoke-house dust, spread by hand, has proved satisfactory for this purpose. One ravine has been left under the old system and is being used for certain observations.

The writer's experience of subsoil drainage on estates by some other workers leads him to emphasise that such drainage is not intended to carry off storm water. The ravines must therefore be levelled and graded so as to allow free passage to the open drains of surface water. The application of oil too over subsoil pipes will ruin the piping and only by complete removal of the oily soil and replacement by fresh can this be remedied. As emphasised elsewhere, in this work as in other spheres, multiple control can never be so effective as competent single executive. It is becoming more and

During these years new estates have from time to time been added to the area of the practice. This has tended to cause periodical rises in the incidence rates over the whole. Chart VIII represents the malarial incidence on these estates which first came under our control in 1922, from that year to 1931.

In 1928 the writer noted a comparative ineffectiveness in the anti-malarial oil mixtures which had previously given satisfactory results. These mixtures were being compounded from the same prescription as before, that is, Diesel fuel oil, solar oil and kerosine in certain proportions. These oils remained the same as regards their burning properties but investigation showed a difference in certain other properties. At a meeting of the Malaria Advisory Board to the F. M. S. Government, the writer (1931) drew the attention of the Board to his experiments on the subject of these mixtures, and Corbett and Hodgkin (1931) confirmed, almost entirely, these experiments under full laboratory conditions. These workers minimized the importance of

volatility, but further stressed the importance of surface tension and viscosity.

The writer has conducted further experiments in the field and, although much work is yet to be done before any final conclusions can be justified, the following figures even suggest a range within which these qualities of the oils should fall for successful anti-mosquito spraying in Malaya.

drained areas. Estate K. (chart IX) has been drained with a view to proper oiling, while estate S. N. (chart X) has been oiled as efficiently as possible over simple agricultural drainage. Both estates have a history of malaria rates in the past of around 100 per cent. per month.

The necessity for constant technical supervision of oiling is well demonstrated in the case of estate H.

CHART VIII

Rates per mille on newly-controlled estates

Population = 500 \pm 150.

Year	Cases	Malaria incidence rate per mille per annum*
1922	3,716	5,133
1923	508	1,229
1924	38	111
1925	16	41
1926	20	38
1927	14	22
1928	20	35
1929	8	14
1930	6	12
1931	6	14

* Note change in scale of graph.

The Asiatic Petroleum Company generously supplied samples of their various oils and very kindly undertook the analysis of a number of mixtures of these oils, some of which had been found successful and some unsuccessful for larval control.

The results of the analyses showed that:—

(1) Although the *flash point* of all successful oils fell within the limits of $81^{\circ} \pm 10^{\circ} \text{C.}$, many unsuccessful oils were also within this range.

(2) The *specific gravity* too showed little relationship to the success, although all successful oils fell within the range 0.870 ± 0.02 .

(3) All successful oils had a *viscosity* (Enggler at 30°C.) of 1.4 ± 0.3 . Some unsuccessful samples of the lighter oils also came within this range.

On this estate the manager elected on his own responsibility to alter the oiling to some practice of his own.

The average malaria incidence rate per month for the previous two years had been 0.3 per cent. After one month from the initiation of the ineffective oiling this incidence was 3.5 per cent. per month, which was again reduced to 0.1 per cent. per month over the succeeding years by proper oiling.

It is always noticeable that the results following such an outbreak are better than those immediately previous. In other words after a manager has been personally convinced of the necessity of the persistent care in the maintenance of the work, his part of it is done much more thoroughly than when it is done merely because his board tells him to do so.

CHART IX Estate B. K.

Month	Malaria rate per cent.	Month	Malaria rate per cent.
January	nil	January	0.4
February	nil	February	0.2
March	nil	March	1.2
April	0.2	April	1.8
May	nil	May	3.5
June	0.8	June	2.8
July	nil	July	0.8
August	nil	August	1.0
September	nil	September	0.8
October	nil	October	nil
November	nil	November	0.5
December	0.2	December	0.9

(4) All successful oils had an *average volatility* within the range $283^{\circ} \pm 7^{\circ} \text{C.}$ The unsuccessful oils were all either less than 234 or greater than 325.

(5) All successful oils had a *surface tension* of 32.6 ± 1.1 dynes per cm. No unsuccessful oil came within this range. All unsuccessful oil mixtures tested were greater than 34.2.

It has been said that oiling should be considered as supplementary to drainage as an anti-malarial measure. Proper results cannot be obtained by oiling unless all water to be oiled has been defined, and the two estates, topographically as nearly comparable as possible, whose monthly figures over one year are shown below (charts IX and X) demonstrate the difference which is to be expected between suitably drained and unsuitably

CHART X Estate S. N.

Month	Malaria rate per cent.
January	0.4
February	0.2
March	1.2
April	1.8
May	3.5
June	2.8
July	0.8
August	1.0
September	0.8
October	nil
November	0.5
December	0.9

Much the same experience has been had in *umbrosus* country. Some years ago a fairly large area dissociated itself from my practice and, arguing that malaria having been absent for many years, the careful maintenance of the anti-larval drainage was no longer imperative, elected to abandon anti-larval drainage and to maintain only agricultural drainage. As malaria reappeared large quantities of oil were used for spraying without however affecting the increase of malaria.

For four years this policy continued, after which time the area reverted to my control and proper anti-larval methods suitable for the conditions of the area were reinstituted.

During these years the annual incidence of malaria rose from 0.9 per cent. per annum to 31.2 per cent.,

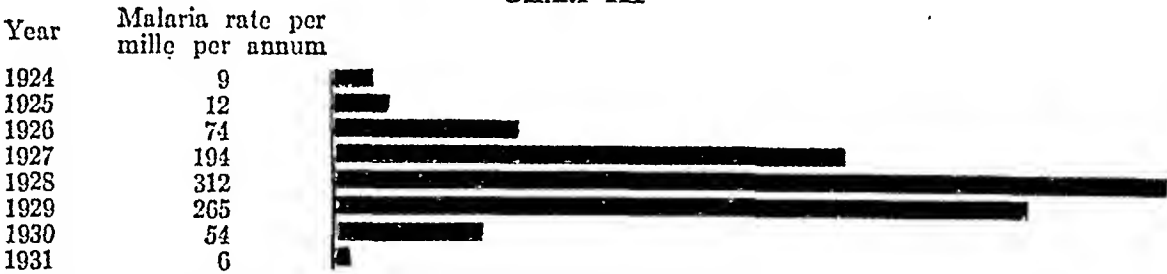
only to fall again to 0.6 per cent. when proper measures were reinstituted (chart XI).

Another recrudescence of malaria in *umbrosus* country occurred in my consultant practice. The estate T. M. had apparently been free from malaria for some thirteen years and had a sharp outbreak in October of one year. Within a month the management gave the malaria incidence as 100 per cent. and at the time of my own

extension of the control to the full half mile but this was done only to the quarter-mile limit. This proved successful although *A. ludlowi* continued to breed at this radius and for some miles beyond. No other vector was implicated in this epidemic.

The measures against *A. umbrosus* elsewhere also remain unchanged, viz, the concentration of all water in sunlit or flowing channels kept free from all surface

CHART XI



Proper anti-larval control was abandoned from the middle of 1925 to the middle of 1929. visit in April of the next year every cooly had malaria. All Europeans had had fever and so many visitors to the estate had been infected that it was being deliberately avoided. The spleen rate, which had been recorded as nil for many years, was 73 per cent.

This case is of interest in more respects than one. The incriminating vector had been considered to be *A. ludlowi* and there is little doubt that this mosquito was associated with the beginning of the epidemic, but on my visit *A. umbrosus* was found breeding in the drains, which in the past had been kept clean-weeded but which for motives of economy were then uncleared. Some *ludlowi* had been found breeding at 16 chains from the lines and these places had been heavily oiled without however effecting the malaria. At my visit however, they were found breeding at 35 chains from the cooly lines. As this area of breeding had been in existence during the years when there was no malaria I advised reversion to the anti-larval methods against the *A. umbrosus* only. Such control also removed the *A. ludlowi* breeding spots at 16 chains.

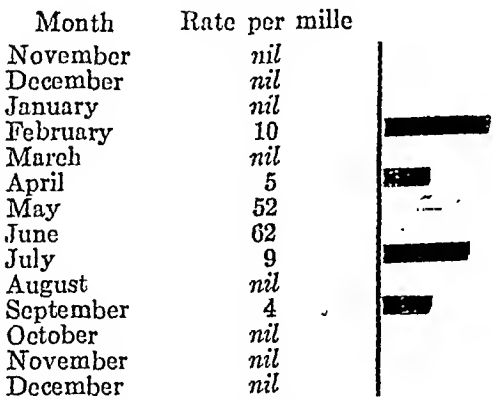
This work was commenced in May. Since August of that year, 1931, to date, October 1932, no case of malaria has occurred.

vegetation. Small epidemics have occurred (e.g., five cases among a labour force of 174 on estate C.) as a result of a long drought providing breeding places for *A. umbrosus*. The drains and wells on the estate were kept scrupulously clean on their sides, but some vegetation existed on the bottom. With water some feet deep in the drains this was of no importance, but as the drought continued the drain became merely a series of small pools shaded by this growth. *A. umbrosus* was found breeding in these pools within 40 yards of the rooms used by the five cases of malaria; one of these patients possessed a vegetable garden at the jungle edge half a mile distant, and he is presumed to have imported the parasite.

Other recrudescences of malaria from this vector have occurred. On estate B. the management closed an outlet drain to the north of the estate in the month of November. A new outlet was provided farther south, but the smaller drains were not regarded and were left to silt up. Water therefore lay in them and soon became shaded by grass. *A. umbrosus* reappeared in them and, as the estate is frequently visited by outsiders, reservoirs were readily available. The malaria incidence is shown in chart XII. The outlet was reopened in the

CHART XII

Malaria incidence rate per mille on estate 'B'



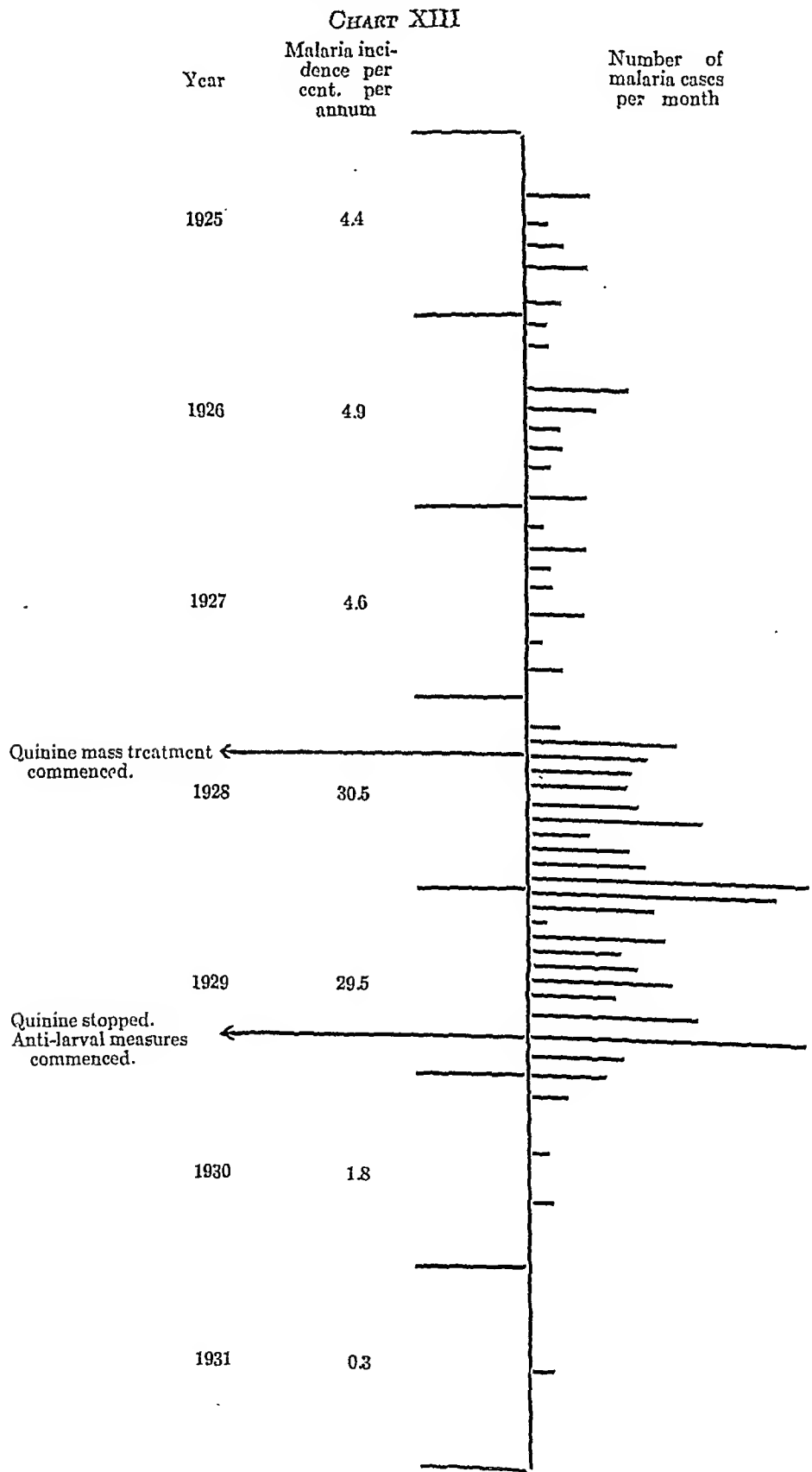
An interesting point is that *A. ludlowi* are still breeding in their usual profusion at a 35 chain radius and for some miles beyond. In view of the suggestion of a longer range of flight of this mosquito this is of interest and fails to support the theory. There is ample fresh water around the lines and adjoining their brackish breeding places.

I recall another case which fails to support this suggestion regarding the flight range of *A. ludlowi*. An epidemic of malaria had occurred in a township which had extended its boundary to within a few hundred yards of the uncontrolled area in which were *A. ludlowi* in their customary abundance. I had advised the

month of June and *A. umbrosus* disappeared along with the malaria.

These results have all depended upon anti-larval methods of control, but the writer does not wish to appear to deprecate the use of chemo-prophylaxis in its proper place. The judicious combination of both clinical and anti-larval methods will no doubt take us further with more ease than either alone, but it is surely the chemo-prophylactic measures which must be supplementary to established anti-larval methods and not *vice versa*.

While of opinion that chemo-prophylaxis may keep the death rate of a small population within reasonable



bounds, or even control the malarial incidence in a small and isolated community, the writer cannot believe that it can ever be successfully applicable to labour forces generally in this country with populations around one thousand and with the constant changes which occur in their individual units.

The writer has made use of chemo-prophylaxis upon occasion and in at least one case has had apparent absolute success in the control of malaria with plasmoquine and quinine. The circumstances of that estate were however exceptional.

In 1928 an experiment was started with drug prophylaxis on an estate which, however, it was impossible to complete.

The estate is situated on the edge of *maculatus* land and extends into *umbrosus* country. Anti-larval control on the flat land had been maintained for many years but *A. maculatus* had never been found on the estate till 1927. This is explained by the fact that the adjoining land on the hilly side of the estate had been controlled and *A. maculatus* had never jumped this barrage to settle on the small area of hillfoot seepage on the estate. In June 1927 however it was first found there. No measures were taken, by intent, and it was not until February 1928 that malaria appeared in epidemic form. This took place one month after a considerable number of the coolies had visited a festival at a neighbouring estate. For 19 months mass treatment with quinine was tried with no success (see footnote).^{*} It had been intended to continue this treatment for two years, this being about the time after which a tentative conclusion of the effectiveness of chemo-prophylaxis can be justified, and then to use plasmoquine. The management however refused to allow further experiment and anti-larval methods had to be instituted. The figures in chart XIII show that during the years 1924 to 1927 the average monthly malaria rate was 0.3 per cent. During the years 1928 and 1929 when quinine was given it was 2.5 per cent. Since anti-larval measures (oiling) have been used the rate as was to be expected has been 0.02 per cent.

In the case referred to above where plasmoquine and quinine appeared to give good results, the locus of the experiment was a small estate being opened up out of a block virgin jungle situated on the foothills and surrounded by impenetrable forest and swamp. No position for housing was possible which would allow of even a quarter mile radius for anti-larval control and *A. umbrosus* was breeding in unusually large numbers. *A. maculatus* had also been found. Adult *A. umbrosus* can still always be found in the temporary hutments erected for the population of 140 persons.

Since its inception the estate has been one hundred per cent. malarious. Visitors even for one night invariably returned infected. Severe cerebral and blackwater cases were frequent. As new planting had to be undertaken new coolies were employed and every one became infected.

Mass distribution of quinine had been undertaken, but in spite of it the spleen rate was 82 per cent. and the stream of severe cases to hospital continued, so that only one-third of the labour was available for work at any given time.

In January 1931 it was decided to try mass administration of plasmoquine. The estate is in the district under the direct charge of the senior assistant, Dr. Lawrence A. Watson to whom, during the writer's leave, all details of the experiment were left.

Owing to the extreme isolation of the estate, personal supervision could not be undertaken and it was decided

to distribute the drug in small doses combined with quinine in capsule. To reduce liability of error administration was effected at each of two musters in the day, on the principle of 'no capsule—no pay'.

The dose of plasmoquine was small but the treatment was continued for 21 days, the dosage being: quinine bihydrochloride, gr. $7\frac{1}{2}$ with plasmoquine gr. $\frac{1}{15}$ (0.004 gm.) twice daily. This treatment was first given in February, 1931. Neither during nor after this treatment has there been any case of clinical malaria whatever.

After three months the 21-day programme of the same doses was repeated. Another three months later a 14-day course of quinine bihydrochloride gr. $7\frac{1}{2}$ with plasmoquine gm. 0.005 twice daily was given. This programme was repeated again in three months time, and again in February, May and August 1932.

Not a single case of clinical malaria has occurred during the twenty months following the first treatment in February, 1931, although in September, 1931, a parasite survey, using thin blood films showed 26 per cent. to harbour parasites.

In August 1932 an examination was made of thick blood films from every coolie resident on the estate. These now numbered only 48. Of these 48 persons 2 only, or 4.16 per cent., showed parasites. Both were subtertian infections although they had had no fever.

At varying periods during the experiment coolies were transferred to a healthy estate where they were kept under observation. In all, the after history of 42 persons was thus recorded:—Of these, 39.5 per cent. were found to harbour parasites on their transfer and were given a 14-day course of quinine gr. $7\frac{1}{2}$ with plasmoquine gm. 0.01 twice daily. There remained still infected 18 per cent. and these were given another similar course. Unfortunately all of them left the estate before further observation could be made.

Among the 42 persons thus transferred from the experimental estate there were 4 double infections of *P. vivax* and *P. falciparum*. After one course of treatment the *P. vivax* in one and the *P. falciparum* in another had cleared up. The other two were free from both.

The small population and its extreme isolation together with its diminishing numbers is felt to have contributed an essential factor to the success of this experiment. It is intended shortly to double the population on the estate and Dr. Watson will report the whole experiment together with the results of this immigration at a later date. As soon as the population is again stabilised the high dosage of quinine will be reduced and an attempt made to assess the relative value of the quinine and the plasmoquine.

REFERENCES

- Barrowman, B. (1931). Anti-malarial Oils and their Specification. *Malayan Med. Journ.*, Vol. VI, p. 7.
 Barrowman, B. (1932). An Example of Anti-malarial Subsoil Drainage under Rural Conditions. *Malayan Med. Journ.*, Vol. VII, p. 160.
 Caldecott, A. (1932). *Annual Report on the Social and Economic Progress of the People of the Federated Malay States for 1931*. Kuala Lumpur: Govt. Press.
 Caldecott, A. (1932). *Selangor Administration Report for the Year 1931*. Kuala Lumpur: Govt. Press.
 Clifford, H. C. (1929). Malay Peninsula. *Encyclopaedia Britannica*. 14th Edition.
 Corbett, G. H., and Hodgkin, E. P. (1931). Laboratory Experiments on the Larvicidal Properties of Mineral Oils. *Bull. Inst. Med. Res. Federated Malay States*, No. 5, p. 20.
 Green, R. (1931). Notes on the Use of Thick Blood Films in the Diagnosis of Malaria. *Bull. Inst. Med. Res. Federated Malay States*, No. 1, p. 10.
 Watson, M. (1921). *The Prevention of Malaria in the Federated Malay States*. London: John Murray.
 Wilson, C. J. (1931). *Annual Report of the Malaria Advisory Board for the Year 1930*. Kuala Lumpur: Govt. Press.

^{*} In administering quinine the writer selects a dose equal to $1\frac{1}{2}$ grains per stone of body weight per diem. For mass treatment an arbitrary adult daily dose of 10 grains was usually selected for a Tamil labour force, and this given to every worker and dependent on the estate. The dose was adjusted for children and infants were given euquinine in condensed milk.

Indian Medical Gazette

FEBRUARY

IMMUNITY IN PROTOZOAL INFECTIONS

BACTERIAL immunity is a subject which has been the centre of intensive study for at least fifty years, consequently a considerable amount of knowledge has accumulated, and, even if this has not been crystallized to the satisfaction of the precise-minded, at least teachers of this subject are in a position to summarize the present-day theories of bacterial immunity without introducing any acutely controversial matter. The same cannot, however, be said of protozoal immunity. Medical protozoology is a much younger science and in some ways a less important one. It is true that the one specific micro-organism which can claim annually the largest number of victims throughout the world is a protozoan, but on the whole the scope of the protozoa for causing disease and death is much more limited than that of the bacteria. The immunological aspect has been considered *pari passu* with the growth of our general knowledge in protozoal diseases and each worker on a special organism or group of organisms has considered the immunity question as applied to his own particular subject, but immunity in protozoal diseases in general has only been taken up as a serious study in comparatively recent years. Many able workers are now involved in this study, but we must give Professor W. Taliaferro the credit of being a pioneer.

There are two schools of thought—or perhaps one should describe them rather as tendencies in the minds of different workers—in this subject. There is the view that protozoa—like bacteria—are parasites, that the body defence mechanism is unlikely to differentiate between micro-organisms of different kingdoms but will exert the full force of its defence mechanism against any invaders, that therefore the immunity response against protozoal infection will be the same as that against bacterial infection, and that we have only to apply the knowledge gained in the one subject to the other. There is the opposing view that, protozoal parasites being animals within animals, there is no immunity response in the ordinary sense of the word, that their death is due to their failure to obtain suitable food or is only incidental following the phagocytosis of the blood cell in which they lie, and that the lytic processes of the body are only active against dead protozoa. The truth, as ever, lies somewhere between these two extreme views.

We have suggested above that the study of immunity against protozoal infection is a young branch of the science of immunology; it enjoys

the advantages and suffers the disadvantages that are always the lot of a younger generation. Workers on protozoal immunity have the general principles of immunity—mostly based on studies in bacterial immunity—already laid down for them, but it often falls to them to demonstrate to other workers, who have accepted the dictates of analogy too readily, that many of these general principles do not apply in the case of protozoa—and to disprove an accepted theory is notoriously more difficult than to establish a fresh hypothesis.

One of the main disadvantages under which the protozoologist, in contradistinction to the bacteriologist, works is that the blood-inhabiting protozoa—and it is with these that practically all work on protozoal immunity has been done—cannot be cultivated so readily outside the human body and that therefore much of his experimental work has to be done *in vivo*. Yet again this is possibly a blessing in disguise and he is on much safer ground when he draws an analogy between the behaviour of a parasite in an animal and that of a similar parasite in man, than when he has to compare the behaviour of the same parasite in man and in a test-tube.

On the other hand protozoa possess certain distinct advantages over bacteria for purposes of immunological study. Those with which we work mainly are larger organisms and therefore they are more easily enumerated, cell division can be observed and the rate of multiplication estimated, and the processes of their phagocytosis and destruction can be more easily followed. Furthermore, there are many protozoal infections which are not fatal to their hosts though the parasites may appear in enormous numbers in their blood; a very good example of such a parasite is *Trypanosoma lewisi* in the rat. It has been shown that in the serum of a rat infected with *T. lewisi* two distinct immune substances develop; the first checks reproduction of the trypanosome and the second has a trypanocidal action. The reproduction-inhibiting antibody is passively transferable and will stop reproduction in the trypanosome in a second rat before this rat's own reproduction-inhibiting antibody has had time to develop. This antibody is not absorbed by the trypanosomes *in vitro* and when washed trypanosomes whose reproduction has been inhibited are transferred to a new uninfected host they will commence reproduction at the ordinary rate. The trypanocidal antibody is also passively transferable, and when injected into a second rat in the early stages of an infection will cut short the infection, but when once the second rat's own trypanocidal antibody has developed no further reduction in trypanosomes can be brought about by the injection of trypanocidal serum from another rat. This suggests that, as in the case of pathogenic trypanosomes, those which resist the trypanocidal action become resistant to subsequent action by this same agency, whether it be drug or antibody.

The trypanocidal antibody, unlike the reproduction-inhibiting antibody, is absorbed by the trypanosomes *in vitro*, and trypanosomes, that have been thus subjected to the action of the trypanocidal antibody, are sensitized, so that when they are injected into a normal rat they are immediately destroyed.

These observations, which were made by counting and measuring the trypanosomes at frequent intervals in a way that would not have been possible had it been a bacterial infection that was being investigated, suggest a fairly complicated antibody mechanism, comparable to that in many bacterial infections; furthermore, the evidence points to this immunity response being mainly of a humoral nature, though admittedly it is claimed by some workers that the final disposal of the trypanosomes is by non-specific phagocytosis.

The plasmodial infections furnish another example of protozoal parasites which lend themselves to investigation by numerical methods. Human malaria is not a good example as the parasites are subject to tissue localization, so that the peripheral blood does not provide a fair sample, as regards parasitic population, of the blood throughout the body; it is for example well known that the segmented forms of *Plasmodium falciparum* do not appear in the peripheral blood at all. Certain avian plasmodia, however, are very suitable for study as they are not subject to tissue localization. A good example is *P. cathemerium* in the canary; here the immunity mechanism is very different from that of *T. lewisi* infection in the rat. There is no reproduction-inhibiting antibody and reproduction follows its regular 24-hour cycle at all stages of the infection. There is, however, evidence of a plasmodicidal immunity mechanism. It has been shown that the rate of multiplication of the parasites represents a 5-fold increase every 24 hours. Now the mature schizont divides into about 15 merozoites so that there is a daily loss of 10 merozoites, which can only in part be accounted for by the side-tracking of some parasites into the sexual stage. This loss is constant, and must be looked upon as evidence of a *natural immunity* in the bird. This 5-fold multiplication of the parasites does not go on indefinitely, and end in the parasitization of the whole erythron and the death of the bird, but after a certain time the process is checked, not by a slowing down of the reproduction cycle, which still goes on as before, but, by elimination of the parasites. There is at a certain stage a sudden very marked fall in the number of parasites, which means that whereas before the loss was represented by 10 out of 15 parasites going astray each day, the survival rate is now represented by one merozoite in, say, 10 rosettes, which means a loss of 149 out of every 150 parasites each 24 hours. It is by no means certain that the casualties all occur amongst merozoites—in fact we have histological proof to the con-

trary; cells of the reticulo-endothelial system are seen containing all forms of malarial parasites in different stages of digestion. Whatever is the change that brings about this state of affairs it must be looked upon as an *acquired immunity*. It is maintained by the host for a long period of time during which super-infection with the same parasite is not possible. There is evidence to show that this acquired immunity, which occurs in all plasmodial infections, is a species-specific if not a strain-specific immunity. It does not appear to be passively transferable, nor do parasites subjected to the action of serum from immune animals suffer any impairment of their power for producing an infection in susceptible animals. What the nature of this immunity is has been a subject of speculation for some time and little positive evidence is available. It has been suggested that the merozoites fail to gain entry into the red cells through some physical change in, for example, the electric charge or surface tension of this cell, and are consequently phagocytosed, or again that the immunity is of a purely histological nature and that the reduction in the numbers of the parasites is brought about by an enormously increased activity of the cells of the reticulo-endothelial system. That there is a great increase of activity on the part of the cells of the reticulo-endothelial system there can be no doubt, but it is uncertain whether this is *post hoc* or *propter hoc*.

In a paper which will be found elsewhere in this number of the *Gazette*, an investigation into the blood cellular reactions to malarial infection in monkeys has been described. The conclusions drawn in this paper are that the histiocyte response is a reaction to the presence of cell debris in the blood, that, though these cells are able to dispose of large numbers of malarial parasites, they are not by themselves capable of eradicating a malarial infection, and that successful immunity reaction is dependent on an associated monocyte response; as these cells are not voracious phagocytes, the suggestion is that their presence is associated with some humoral change in the serum which is possibly of the nature of an opsonin. However, the positive evidence with regard to immunity in plasmodial infections in general is that it is mainly a cellular response.

These few examples of investigations into the nature of immunity in protozoal infection suggest that these infections are particularly suitable for certain types of investigation, and that, if in the past protozoologists have gained much assistance from general immunological principles mainly worked out on bacterial and spirochætal infections, reciprocity is possible, and that by these or similar protozoal investigations we may add to, or revise, these general principles in such a way as to lead to a better understanding of immunity in bacterial and spirochætal infections also.

THE NEW YEAR'S HONOURS

THE names of medical men and women that appear in the New Year's honours list will be found elsewhere in this number. It is our usual practice to publish the honours list and to congratulate the recipients, but we do not as a rule select any names from this list for special comment. We feel confident that our departure from this rule to make a short reference to the K.C.I.E. conferred by His Majesty the King-Emperor on Major-General J. W. D. Megaw, C.I.E., K.H.P., I.M.S. will not only be forgiven, but will be warmly approved by all of our readers in India.

In the early years of his service in Calcutta Sir John made a great reputation as a physician; at Lucknow, where he was the professor of pathology and principal of the Lucknow Medical College, and later in Calcutta, where he held the post of the director of the Calcutta School of Tropical Medicine for 7 years, he was a most successful and popular teacher; as a medical investigator he has world-wide reputa-

tion, and in each of the two provinces, the Punjab and Madras, where he was head of the medical department, he left permanent marks of his great administrative ability. His appointment as Director-General, Indian Medical Service, three years ago was the natural corollary to his earlier distinguished service and was a surprise to nobody. It would perhaps be out of place, and it is also quite unnecessary, for us to expatiate on the service Sir John has rendered, and fortunately still is rendering, to the medical services and profession in India in this very difficult period.

We ourselves have a special interest in any honour that is conferred on Sir John, because he was for seven years editor of this journal, and we believe that this most successful editorship, during which the journal more than doubled its circulation, cannot be accounted as the least important of the services which he has rendered to medicine and the medical profession in this country. We offer him our heartiest congratulations.

Medical News

THE OPENING CEREMONY OF THE ALL-INDIA INSTITUTE OF HYGIENE AND PUBLIC HEALTH, CALCUTTA

THE All-India Institute of Hygiene and Public Health was to have been opened by His Excellency the Viceroy, but unfortunately Lord Willingdon was indisposed and was unable to attend. The ceremony was performed by His Excellency Sir John Anderson, the Governor of Bengal, in the presence of a large gathering of distinguished visitors, on 30th December, 1932. His Excellency was first introduced to the construction committee of the Institute and then conducted to the large auditorium where the visitors were assembled. Lieutenant-Colonel A. D. Stewart, I.M.S., the Director of the Institute, opened the proceedings by giving a short sketch of the public health policy in Great Britain, which he said had to a large extent provided the inspiration and pattern to other countries in the framing of their public health policies. He then proceeded to discuss the position in India, and of the special place of the Institute in this scheme. He said,

'The opening of this Institute marks a very definite stage in the evolution of public health in India, and it may be interesting on the one hand to trace shortly the events which have led up to its inauguration, and on the other to envisage the part which it is hoped it will play in the future development of public health and state medicine in India. India is at present faced with a coming fundamental change in its constitution and administration. As Sir George Newman has pointed out, development and progress in public health in England have always followed closely on political advancement and change. In India, evolution in these matters has been slower, but we may be assured that, if the present impending changes in India are pregnant with possibilities and opportunities of extended power, responsibility and action to Indians, so will the demands of public health problems for consideration and action become more and more insistent and pressing on the future legislators and administrators of India. Such experience and wisdom and foresight as become

available for general government and administration will also be applied to health problems; for government and public health and welfare are inextricably connected. In envisaging policies and schemes of public health administration in India, we are prone to consider the history of the English system. Though state medical services of the various civilized countries have developed along very different lines, it is interesting to note that the English system has formed the basis of most of these organisations. The English state medical service was first based on the Elizabethan Poor Laws and was at first completely parochial. As the result of the work of Chadwick about 1840, it later became largely centralized. From 1875 began what one may call modern decentralization and a development of the principle of local responsibility, which has gradually developed and which finds definite expression in the Local Government Act of 1929. This Act enlarges and unifies local responsibility in every branch of state medicine and public health. Such decentralization is only possible in a highly organised community, and where public education in health matters has advanced to a point at which the intelligent co-operation of the community as a whole can be counted upon. It is not a principle to be blindly applied as such, but represents a stage of definite development.

The medical officer of health has always been considered the mainstay and prop of the state medical service. The great Public Health Act of 1875 in England made it compulsory on every local authority to appoint a medical officer of health and since 1888 the possession of a diploma of public health has been practically essential. Facilities for specialised training have been available in the British medical schools and universities for over 50 years and have received, particularly lately, special attention from the General Medical Council of Great Britain. Sir John Simon, who served the Local Government Board of England as its Chief Medical Officer from 1855 to 1877, may be taken as the prototype of the English public health scientific official—'always an administrator, never a legislator, forced to carry out his conceptions under the cloak of another's authority;

developing caution and perspicacity in observing trends of thought which provide the security and at the same time the danger of sterility in this sphere to-day.' The spirit of Simon is still that of the successful medical officer of health to-day; contentment with a judicious compromise and the accumulations of small effects in a big result.

Indian public health policy may be said to have commenced in 1857 with the taking over of the civil administration from the East India Company by the Crown. As the result of a Royal Commission appointed in 1860 to enquire into the excessive mortality amongst the civil and military populations, sanitary commissions were appointed in the main provinces. Departmental jealousies and other causes however prevented much being done (except in Madras where the appointment of sanitary inspectors became obligatory in municipalities) and the commissions up to 1906 consisted only of 1 officer who had no staff and few responsibilities or opportunities.

The arrival of plague in Bombay in 1896 awakened the Government of India to its responsibilities and in 1912 a notable advance was made by the giving of grants from central to provincial revenues for the purpose of strengthening the central provincial sanitary staff and for making a start with the provision of district and municipal officers of health. Provinces were allowed to develop their own policy in the appointments of the latter class of officers. Some, like Bengal, adopted the English method of letting local bodies appoint their own health officers, while others mostly appointed a provincialised staff of district and municipal health officers. Provision for instruction and training in health work was meagre and up till 1914 practically all health appointments were held by men possessing British diplomas of public health. While such were suitable for administrative appointments, it was obvious that a training in English conditions could not adequately meet the needs of those actively engaged in practical health problems of Indian districts and towns. The need for such training in India became imperative. Though most Indian universities were prepared to grant diplomas in public health, adequate facilities for training did not exist. In Bengal where district and municipal health officers became compulsory in 1914, temporary arrangements for training were made by the Director of Public Health.

At this time Sir Leonard Rogers was actively engaged in his scheme of establishing a School of Tropical Medicine in Calcutta and his remarkable perspicacity quickly grasped the desirability of including advanced teaching of hygiene in the School of Tropical Medicine. A full-time professor of hygiene was therefore included in the staff of the School, which was affiliated to the University of Calcutta for the purpose of instruction for the diploma of public health. Facilities for special instruction in hygiene were also provided at some other Indian universities.

The Reforms Act of 1919 by removing the advisory control of the Government of India and placing on provincial Governments full responsibility for public health in every respect within the province acted in some respects as a stimulus to Local Governments to enunciate and develop sanitary policies. A few did so, though political dissensions prevented full advantage being taken of this opportunity. In the Calcutta School of Tropical Medicine classes of annual training for the diploma of public health were held and the numbers seeking admission from all over India increased. It became evident that these classes were fulfilling a definite requirement outside Bengal, and that as public health policies and activities developed in India and increasing responsibilities were being assumed by Indians, there should be some institution of an All-India character which would not only train graduates for the University D.P.H. but would provide those already engaged in public health work with facilities for training and for independent higher research. Such an institute would take up investigation in Indian health problems

and questions and would moreover help to co-ordinate public health work all over India and might assist Local Governments and others in any manner possible.

These ideas and possibilities impressed themselves on Major-General Megaw and Major-General Graham, at that time Director of the School of Tropical Medicine and Public Health Commissioner, respectively, and were expressed clearly on several occasions in their annual reports. Dr. Carter of the Rockefeller Foundation during his frequent visits to India was enabled to study medical and public health questions very closely at first hand, especially in their educational aspects. Independently he arrived at the same conclusions as General Megaw and General Graham, and when he found responsible opinion in India in agreement with his, he was enabled to lay before the Rockefeller Foundation his opinions and proposals, which prompted the Foundation to make in 1928 their munificent offer to the Government of India. This offer resulted in grateful acceptance and the first fruits of the Foundation's munificence are seen in this building which is now ready to start its work. On the use which India makes of this Institution will depend its ultimate benefits. India stands now at a new gateway of increased freedom, responsibility, duties and I hope increased health. During the next few years, it will be my duty as Director along with my staff to study and observe the changing conditions and changing systems of administration in India, to devise courses of training and create opportunities for research and methods of practical application of knowledge and research for the development and progress of public health in India. Our success must depend largely on how Indian opinion and Indian administrators face their new opportunities and on the spread of knowledge, and on the growth of responsibility and co-operation in the masses of the Indian people. The opening of the Institute therefore happily coincides with the opening of a new era in the history of India and it would have been very fitting and appropriate that His Excellency the Viceroy who will inaugurate the latter should open the All-India Institute of Hygiene.

It is a matter of great regret that His Excellency the Viceroy is unable to be here to-day owing to illness, but we are fortunate indeed in having your Excellency here to open the building in his absence.

Before asking your Excellency to declare this Institute open I would ask your gracious acceptance of a gold key from Sir R. N. Mookerjee as a memento of this occasion.

Sir Rajendra, whose intense devotion to the promotion of the welfare of his countrymen is well known, has taken a personal interest in the construction of this building much beyond that of his merely being the head of the firm which built it. From the very first the object of the building appealed strongly to Sir Rajendra and for his great personal interest and his practical assistance throughout we cannot thank him enough. I would therefore ask that your Excellency will permit Sir Rajendra to offer you a gold key.

Sir R. N. Mookerjee, K.C.I.E., K.C.V.O., then presented to His Excellency a golden key. Sir John Anderson accepted the key and thanked Sir Rajendra. He continued,

'His Excellency the Viceroy has asked me to convey to you all his great regret that owing to indisposition—not I am glad to say serious but such as to make it imperative that he should stay indoors, he is unable to be present here to-day. In the circumstances he has requested that I should perform in his stead the opening ceremony of the All-India Institute of Hygiene and Public Health. While I fully share the regret that you must all feel at His Excellency's enforced absence, I need hardly tell you that I count it a great privilege to be able to perform this function.

Every important country has in recent years become alive to the necessity for an institution of this nature and, for reasons which have been lucidly explained by Colonel Stewart, India has now wisely followed suit.

This fine building in which we are gathered, the site on which it stands, and its complete equipment, much of which has yet to be installed, represent a munificent gift to India from the Rockefeller Institution—the total value of which amounts to approximately 18 lakhs of rupees. The world-wide benefactions of the Rockefeller Foundation are certainly without any parallel, not merely because of their unrivalled generosity, but also because of the extraordinary care and forethought which is taken to ensure that the best possible use is made of the huge sums which are distributed every year. The members of the Foundation insist on making a thorough preliminary survey of every field of activity in which their help is needed, and, acting on this principle, they sent to India one of their highly skilled experts, Dr. Carter, who made an exhaustive and sympathetic study of medical education in this country. As the result of his report, the Foundation made their generous offer of this All-India Institute of Hygiene and Public Health. What they stipulated in return was that the Institute should serve the whole of India, that the Government of India should undertake the responsibility for the adequate maintenance of Public Health teaching to be organised in six sections in co-operation with the School of Tropical Medicine, and that the Scientific control of the Institute should be entrusted to a Governing Body constituted in such a way as to ensure single-minded devotion to scientific endeavour by a staff chosen solely with regard to its competence. These conditions, far from being irksome restrictions upon the activities of the Institute, are useful safeguards for securing its permanent value to the people of India. The Government of India gratefully accepted the gift and entered into an undertaking to comply with the conditions laid down by the Foundation. It is most unfortunate that owing to the financial situation they have had to start the Institute with four sections only instead of six as was originally intended, but we hope that it will not be long before this deficiency can be made good.

It may be appropriate, ladies and gentlemen, that I should here say a few words about the School of Tropical Medicine and Hygiene which forms the historical background of the new Institute as well as an integral part of the whole scheme. This School stands as a monument to the energy of Sir Leonard Rogers, whose great achievements in combating tropical diseases are known throughout the world. It was expected that his School would provide ample accommodation for the requirements of the teaching and research staff for many years, but the rapid growth of their activities soon showed its Director that a separate Institute of Hygiene was essential for the completion of the scheme. I am confident that history will now repeat itself and I feel that there could be no happier augury for the future of the Institute than the great success achieved by its forerunner—the School of Tropical Medicine. It is indeed gratifying to my Government to find that their action in assuming responsibility for the School has paved the way for the establishment of this organisation, which will supply the needs not merely of Bengal but of the whole of India.

A special word of thanks is due to Major-General Megaw for the unflinching interest and industry with which he has worked for the completion of this beneficent scheme. I wish also to thank all the members of the Constructional Committee for the efficient manner in which they have performed their voluntary task. The work was completed within the specified time and within the estimated cost. In achieving these happy results the Committee were greatly helped by Sir Rajendranath Mukherji, the head of the firm which constructed the building, who, I know, regarded the erection of this Institute as a labour of love rather than as a commercial undertaking.

Colonel Stewart has happily stressed the point that the foundation of the Institute coincides with the opening of a new era in the history of India. India

is now about to enter the gateway to further constitutional advance. Great opportunities entail great responsibilities, not lightly to be discharged, and functions which will influence profoundly the future welfare of the country and its people. But I am confident that the experience gained since the introduction of the Reforms Act and the establishment of Local Self-Government has prepared administrators and legislators for the assumption of the onerous duties that lie ahead of them. Let them remember that good government and the health and welfare of the people march hand in hand. It is not too much to say that the future of this Institute will depend equally upon the wisdom and vision of the administrators of the country and upon the willing co-operation of the people.

India owes an enormous debt of gratitude to the Rockefeller Foundation for their munificent gift and His Excellency the Viceroy bids me assure the Foundation that the Government of India will make the fullest possible use of the gift as a means of promoting the advance of Public Health throughout the land. The Staff of the Institute will, I know, leave nothing undone in the discharge of their duties to fulfil in every way the objects for which it has been established. I have to convey to them, on behalf of His Excellency the Viceroy, his sincere good wishes in the great task that lies ahead of them and an assurance of his continued interest in their welfare.

I now have the honour to declare open the All-India Institute of Hygiene and Public Health.

After this His Excellency made a short tour of the building and departed. The guests were then asked to inspect the building.

THE INDIAN HONOURS LIST

1st JANUARY, 1933

The following are the names of medical workers in the Indian Honours List of date 1st January, 1933. We would offer them our congratulations.

K.C.I.E.

Major-General J. W. D. Megaw, Director-General, Indian Medical Service.

C.I.E.

Major-General W. C. H. Forster, Surgeon-General, Bombay Government.

Colonel J. N. Walker, Director, Medical Department, Nizam's Government.

Lieutenant-Colonel R. B. S. Sewell, Director, Zoological Survey of India.

Kaiser-I-Hind Medal, First Class

Miss Charlotte Rose Greenfield, in-charge, St. Margaret's Hospital, Poona.

Robert Harold Goheen, in-charge of the American Presbyterian Mission Hospital at Vengurla, Ratnagiri District.

Rai Bahadur

Lakshmi Narain Rai, lately Member of United Provinces Medical Service, Benares.

Hargovind Sahai, United Provinces Medical Service, Lecturer, King George's Medical College, Lucknow.

Rao Bahadur

Tinnevely Subba Ayyar Tirumurti, Professor of Pathology, Medical College, Vizagapatam.

Sardar Sahib

Bhai Hira Singh, Civil Surgeon, Campbellpur, Punjab. Pishora Singh, Sub-Assistant Surgeon, Yenangyaung Magwe, Burma.

Khan Sahib

Sayid Wahi-ud-din Haider, Civil Surgeon, Unao, United Provinces.

Rai Sahib

Hridindra Nath Ray, Medical Practitioner, Mymensingh.

Jasoda Nand Srivastab, Civil Surgeon, Basti, United Provinces.

Triugi Narayan Lal, Sub-Assistant Surgeon, Insein, Burma.

Balmakund Naik, Health Officer, Puri Municipality, Bihar and Orissa.

Kalipada Mitra, Assistant Surgeon, Bihar and Orissa.

Subedar John David Bailly, Sub-Assistant Surgeon in-charge of Sind Malaria Enquiry under the Malaria Survey of India, Kasauli.

Rao Sahib

Vengappier Subrahmanyam, Superintendent, Office of Director, Public Health, Rangoon.

Narhar Ramchandra Ghatge, Subordinate Medical Service, Officer-in-sub-charge of West Hospital, Rajkot, Western India States.

Shankar Rangji Jadhav, in-charge of Panwel Dispensary, Kolaba District.

QUARTERLY BULLETIN OF THE HEALTH ORGANISATION OF THE LEAGUE OF NATIONS

Two more numbers (nos. 2 and 3) of this important publication have been received. They contain amongst other matter, two authoritative articles on medical education in France and Germany, respectively. In the first of these two numbers there is a paper on malaria in Siam, a report of a study carried out by the request of the Government of Siam, also the report of the commission on the fumigation of ships.

This publication is one of primary importance to all public health organisations throughout the world, and a copy should at least find its way into the office of every provincial director of public health and port health officers in this country.

KING EDWARD VII'S CONVALESCENT HOME FOR OFFICERS AT OSBORNE

OSBORNE HOUSE, once the favourite residence of Queen Victoria, is situated in The Isle of Wight, between Cowes and Hyde. This one-time Royal residence was given by King Edward, in memory of his illustrious mother, Queen Victoria, to the nation to be converted into a convalescent home for officers of the navy and army; this was at a time when there were only two services. To-day, officers of all three services, as well as of the Indian Army, are received at the convalescent home on the recommendation of the respective directors-general of the medical departments of these services.

The accommodation at Osborne provides for fifty officers, at a very moderate charge, which includes all medical attendance, with such special treatment as massage, diathermy, ultra-violet rays and other electrical treatment, and special dieting. A staff of London consultants pay regular visits, and the mild and equable climate is ideal for convalescents from the tropics. There is a certain amount of accommodation for officers' wives in a private hostel on the estate.

Special features of the grounds are the fine lawns with their tennis and croquet and the picturesque trees, many of which were planted in commemoration of the visits of Royal and illustrious personages. These trees include the magnificent avenue of evergreen oaks at the Royal entrance and Californian pines and other rare trees, all of which are in excellent state of preservation.

Bathing facilities are provided by Osborne Bay, the private beach where Queen Victoria spent much of her time, and circling which a promenade was built to enable her to drive in her pony carriage along the sea front.

There is also a small golf course. In the house there is an excellent library and a billiard room.

We can think of no more ideal place for officers, who have had to take leave from this country on account of ill health, to spend the first few months of their leave. Nobody need be alarmed by the words

'moderate charge'; this is unfortunately an expression which has now been adopted by luxury hotels, but, though we have not any exact figures to quote, we understand that the terms are really moderate and that the impecunious officer going home from this country will find it cheaper than living in a boarding house. In addition he will have all the advantages of a first-class nursing home, combined with those of a 400-acre country club in a glorious situation.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of February, 1883, Vol. XVIII, p. 47)

PETTENKOFFER's views on the subject of cholera causation are well known, and have frequently been presented and commented upon in this journal. Stated briefly, he holds that certain local and seasonal conditions and individual predispositions are necessary for the effective action of the cholera infection.

* * * * *

He inclines to the belief that the cholera germ is a fungus belonging to the *Schizomyces*, but seeing that their presence is universal, search must be made for a special fungus or for special conditions which confer on an innocent fungus virulent or lethal properties.

* * * * *

After reproducing his early hypothesis he says:—'It may be sufficient to point out that from that time to this I have never found myself in opposition to the parasitic theory; I have striven solely and always against the theory of simple contagion which, in my opinion, is erroneous. I have also endeavoured to obtain for local influences their proper position in epidemiological views, and also to hold out goals of the richest promise to experimental fungology in which I cannot myself take an active part. When I consider the results of the work of the Cholera Commission in the light of the prevailing fungus theory of the present day, I might hold it as most probable, seeing that, as I have before said, cholera is no putrefactive poisoning, that intercourse with places in which the disease is endemic or epidemic spreads an organism (x) which causes cholera in some way unknown to us at present. The poison, however, when brought into other localities without losing its poisonous property, can only propagate itself when it finds in that place a suitable substratum (or nidus) (y), which has its origin in the ground, and serves, so to speak, as nutriment or a host, and which is either already in man himself, or, as seems to be more likely, is in the ground, and from thence attaches itself to dwellings situated on the ground, or to objects to be found therein. Again in cases in which outbreaks of cholera appear to rise without the intervention of the soil, as for example on board ship, the simultaneous presence of the germ (x) and the substratum (y) arising from the land, must be admitted.'

Current Topics

Recent Developments in Immunotherapy

By LAWRENCE P. GARROD, M.B., M.R.C.P.

(From the *Practitioner*, October, 1932, Vol. CXXIX, No. 4, p. 471)

THERAPEUTIC immunization is of two kinds: 'active', bacteria or their products being introduced into the body with the expectation of evoking a state of resistance comparable to that following spontaneous infection; and 'passive', which involves the use of a serum containing already formed those substances by which it is believed that infection is resisted or overcome. Each of these methods is subdivisible, the former according to whether the material used contains actually living bacteria, dead bacteria, or bacterial products; the latter

according to the nature and mode of action of the specific substance in the serum. Some examples of these methods are familiar, others have by no means yet received the general recognition which they deserve. It may therefore be useful to review some of the newer methods, classifying them under the headings already indicated.

ACTIVE IMMUNIZATION

(1) *By means of living bacteria.*—There can be no question that when it is possible to practise immunization by this method, the state of immunity which results is superior to that obtainable by any other. This is to be expected, since the proceeding is the nearest approach to an actual attack of the disease. It is only feasible when the capacity of a micro-organism for multiplying in the body can be greatly diminished; this change can sometimes be effected by exposing it to unusual or unfavourable conditions, whether *in vivo* or *in vitro*. Habituation to a different animal host is an example of the former method, and is the basis of two important and reliable methods of immunization: vaccination against smallpox is inoculation with living smallpox virus which has lost its capacity for producing this disease in the human being by repeated transference among calves, and the prophylactic treatment of rabies depends on the use of living rabies virus reduced in its capacity for attacking man and dogs by passage in rabbits, although here attenuation is secured further by drying the rabbits' spinal cords in which the virus is contained. Among ordinary bacteria, attenuation results from prolonged artificial cultivation, from cultivation in media which, while still permitting growth, contain some inimical substance, and from cultivation under abnormal physical conditions, such as high temperature or pressure; such treatment has been applied in the past to produce living, but nevertheless safe, vaccines for immunizing against anthrax, cholera and typhoid fever.

There is a comparatively new example of this method which has enormous possibilities, although it is still too early to judge whether they will be fulfilled. B. C. G. (Bacille Calmette-Guérin) is a strain of the tubercle bacillus which has been grown since 1908 on a medium containing bile, and has consequently lost much of its capacity for producing disease. Even the guinea-pig, in which inoculation with the smallest numbers of ordinary tubercle bacilli is followed by a progressive and fatal infection, can withstand inoculation with it; a lesion results which is circumscribed, and the animal recovers.

The practice advocated by Calmette is the administration of three doses of living bacilli by the mouth to infants during the first ten days after birth; phagocytosis is believed to take place in the alimentary canal, the bacilli being carried to neighbouring lymphoid tissue and there destroyed. The treatment is undertaken at this extremely early age for two reasons: (1) the bacilli are said to be more readily removed from the bowel during the first fortnight of life, and (2) inoculation, to be effective, must precede natural infection. The treatment has now been applied to upwards of 100,000 infants in France, mainly those born in tuberculous families and therefore exposed to infection at an early age. This is naturally a method of which the results can only be assessed after the lapse of years, and then only with difficulty. From the statistical point of view, Calmette's results to date are said to be unconvincing. From the theoretical standpoint the method is open to two serious objections: (a) that an unmeasurable dose is being given, since the degree of absorption from the bowel and the extent of subsequent multiplication of the bacilli are beyond control, and (b) that the organism itself may be capable of regaining virulence; this aspect of the subject has recently been reviewed by Dreyer.

Nevertheless, the fact remains that living tubercle bacilli have been administered to hosts of children with at all events few untoward results, and that this

proceeding should theoretically secure some degree of immunity. There is certainly at present no more hopeful method of dealing with a disease which has defied forty years of varied efforts at specific therapy. It is not to be forgotten that the immunization of children is only one of two uses to which this method may be put. If it be granted that resistance to tuberculous infection can be increased by means of B. C. G., even were the risks of effective dosage too great to justify its use in infants, there remains the important possibility of immunizing calves among which a small mortality would constitute a less serious objection. The unsatisfactory state of the milk supply in this country and the amount of disease in childhood attributable to this cause have recently been discussed in this journal by Moynihan. There is therefore no need to recapitulate the facts, nor would it be profitable to discuss the merits of pasteurization as a remedy, beyond saying that tubercle bacilli in 'pasteurized' milk are by no means always dead. Viewed from whatever standpoint, the prevalence of tuberculosis in cattle is a grave danger, and if inoculation of calves with B. C. G. can free the dairy herds of this country from tuberculosis, the achievement will be second in importance only to the successful immunization of children themselves.

There are no other established uses for living bacterial vaccines; the method has potentialities of danger which have discouraged its application. It is nevertheless tempting to speculate on the possibilities of treating resistant chronic inflammatory conditions by this method, such, for instance, as long-standing nasal infections due to bacteria which in many cases have little general invasive power, and would therefore not be expected, especially if attenuated, to give rise to any progressive lesion if injected into the subcutaneous tissues. This is a field which remains almost wholly unexplored.

(2) *By means of killed bacteria.*—In the use of ordinary bacterial vaccines, the position remains much as it has been for many years. Reasonably effective prophylaxis can be assured against certain specific infections, such as enteric fever. The comparative uncertainty of prophylaxis for colds and influenza is no doubt largely due to the multiplicity of bacteria concerned, many of which may be represented inadequately or not at all in the vaccine used. If we accept the proposition that some, at least, of these infections are due to a virus, failure is hardly surprising. There is, however, one quite specific infection in which preventive inoculation deserves a wider application, at least until its value can be better appraised; on the appearance of whooping-cough in a family or school, the remaining children may be treated with a *B. pertussis* vaccine with at least an expectation of mitigating the severity of the disease should they contract it. This is a conservative statement in comparison with those of French writers (Pierret), who claim absolute prevention following prophylactic administration and amelioration even if the vaccine be given during the course of the established disease. The discrepancy between these and certain English results, possibly attributable to differences in technique, require that the method should be more fully investigated.

(3) *By means of bacterial products.*—Substances produced from bacteria in a great variety of ways have been used for the purpose of immunization. The method among all these which rests on a sure foundation is the use of soluble toxins. In considering infections from an immunological standpoint a sharp distinction must be drawn between those due to bacteria which produce such a toxin and those which do not or which, at all events, have not so far been shown to do so. In the former, the condition is a toxæmia in the true sense; a demonstrable toxin is produced which is carried to distant parts of the body, whereas the bacteria forming it remain strictly localized in a lesion which in itself may be comparatively trifling; of this type of infection, tetanus is, perhaps, the best example. The outcome of infections of this type depends immediately

not so much on any capacity to deal with the bacteria themselves as on the formation or supply of the antitoxin which will neutralize their toxin. Similarly, preventive immunization must consist in administering not bacteria, but toxin.

It would doubtless be possible to immunize by this method against any of these infections, but tetanus, botulism, gas gangrene and Shiga dysentery are not conditions against which it is usually worth while to secure anticipatory protection. There remain, however, diphtheria and scarlet fever, the former the earliest and most extensively studied of these true toxæmias, the latter admitted to this category only within the last ten years. Susceptibility to either of these infections can be determined by the intracutaneous injection of a small amount of toxin (the Schick and Dick tests) and immunization of those so shown to be susceptible can be carried out by subsequent subcutaneous injections of toxin itself for scarlet fever, of toxin mixed with antitoxin or otherwise modified (since pure toxin is too dangerous) in the case of diphtheria.

It would be out of place here to attempt to review the great volume of work which has been done during the past ten years in attempting to perfect this method. Its objects, especially in the case of diphtheria, have been to evolve a product which will immunize with maximum regularity after a minimum number of injections, which shall be followed by the least possible local and constitutional reactions. The later developments in this direction depend on Ramon's observation that treatment with formalin deprives diphtheria toxin of much of its actually toxic properties without altering its capacity to immunize; this modified toxin, supposed to be identical with Ehrlich's 'toxoid', has been used alone and, more recently, in combination with antitoxin. T. A. F. (Toxoid-antitoxin floccules) consisting of the precipitate obtained when the two are mixed under certain conditions. Of several preparations now available, each may be depended upon to convert at least 90 per cent. of Schick-positive reactors into negatives after a course of three injections which rarely cause even a trivial disturbance.

It is natural to expect that immunity to a grave disease can only be purchased at the expense of an effort on the part of the body which shall entail at least some temporary incapacitation, but, although this is true of some methods of prophylaxis, the price to be paid for immunity to diphtheria is usually no more than the trifling discomfort of the injection itself. That the immunity conferred has adequate permanence is shown by Parish and Okell's re-testing of 440 children from one to seven years after immunization; 95 per cent. were still Schick-negative. Even in the individual who reverts to the Schick-positive condition there is reason to believe that a state almost equivalent to immunity exists, since it has been shown that when once the body has responded to diphtheria toxin, the slightest further stimulus at a later date is followed by the rapid production of antitoxin in considerable amount: in one such case observed by O'Brien, the minute amount of toxin introduced in the Schick test itself had this effect, a second re-test performed later being negative.

Ideally, the universal immunization of young children, at all events among urban populations, is the consequence to which these advances should lead. Public apathy or hostility will probably stand in the way of this development for years to come, and there are still many areas in which facilities for the treatment are not provided. The individual practitioner, therefore, has frequent opportunities of securing protection for individuals, families or communities; that hospital nurses and school children should be tested and, if necessary, treated, is now becoming widely recognized.

PASSIVE IMMUNIZATION

Therapeutic sera are of three chief kinds, of which two are familiar and may be considered briefly.

Antitoxic serums.—In a limited number of diseases to which reference has already been made, the phenomena

of the illness are due chiefly to the absorption from the lesion of a toxin which can also be produced by the growth of the causative organism *in vitro*. Toxin so produced, when injected into animals, excites the formation of an antitoxin which will neutralize very large amounts of toxin, and the serum containing it therefore constitutes a powerful therapeutic weapon, the capabilities of which are accurately measurable. Of the use of these serums in diphtheria, tetanus and some other infections, there is little new that need be said. A rather different and more debatable position exists in connection with the use of scarlet fever antitoxin. We know now that scarlet fever is a streptococcal infection, that the rash is due to the formation of a toxin, that this toxin can be manufactured *in vitro*, can be used for a susceptibility test and for prophylactic immunization just as in the case of diphtheria, and when injected into animals produces an antitoxin. That this antitoxin furnishes appropriate treatment for scarlet fever there is no doubt, but it is being used extensively for the treatment of severe streptococcal infections of other kinds, and its applicability to these is a matter of some difficulty and interest. The 'unitarian' view of the streptococci recently advocated by Okell in a comprehensive review of the part played by these organisms in human disease, regards the hæmolytic streptococci as essentially one race, of which different members vary in their capacity to produce certain effects. Thus, the streptococcus in a case of scarlet fever is one which produces enough of the 'erythrogenic' toxin to cause the rash characteristic of that disease; in septic infection elsewhere, the invasive and pyrogenic activities of the organism predominate, although the red lymphatics sometimes seen in lymphangitis may be taken as evidence that the erythrogenic toxin is also being produced. Scarlet fever antitoxin can do no more than neutralize this one toxin, but assuming that this is produced at least in some amount that all hæmolytic streptococci, its neutralization may just serve to turn the scales in the patient's favour. That life may thus be prolonged and the infection localized in streptococcal septicæmia in rabbits has been demonstrated by Parish and Okell. A preliminary Dick test, where the time can be afforded, is suggested by Okell for distinguishing those cases in which antitoxin cannot be expected to help (*i.e.*, giving a negative result) from those which it may benefit.

It should be added that *Staphylococcus aureus* is now known to produce an exotoxin, and that the antitoxin treatment of severe staphylococcal infections is in the experimental stage; it is too early yet to assess its results.

Anti-bacterial serums.—These are serums containing or supposed to contain antibodies which act on bacteria themselves. In contrast with antitoxic serums, their activity is singularly difficult to estimate, whether experimentally or clinically. The anti-streptococcal serum, to be distinguished clearly from scarlet fever antitoxin (one being prepared by immunizing animals with the organism, the other with its toxin), which was formerly much used in the treatment of streptococcal infection, is an example. Convincing evidence of the efficacy of many of these serums is lacking, and their mode of action is often obscure. In cerebrospinal fever we have one disease which is clearly amenable to treatment with an efficient serum of this type, and it is possible that pneumonia will prove to be another example when the Felton concentrated serum has been more fully evaluated. With this possible exception, no new anti-bacterial serums of certain efficacy have recently been produced.

Convalescent human serums.—A new method having far-reaching possibilities was brought to light when Nicolle and Conseil showed in 1916 that measles in a susceptible subject exposed to infection could be prevented by the injection of serum from a recently-recovered case. Debre, seven years later, was responsible for the observation that when given at a later stage, the effect of the serum was to diminish the severity of the

attack. This proceeding he christened 'Sero-attenuation', and in healthy patients it is preferable to complete protection in that the ensuing mild attack is succeeded by lasting immunity.

The practical opportunities afforded by this method have been discussed recently by Gunn and also by Nabarro and Signy, Stocks; it therefore appears necessary only to recapitulate the main facts. Using the serum of recently-recovered cases, a dose varying from 3 to 12 c.cm., according to the age of the patient receiving it, will protect completely if given during the first five days of the incubation period, or modify the attack if given between the sixth and ninth days. Adult serum, if the donor has had measles in childhood, is effective in approximately double this dosage; whole blood may be given if a parafined syringe be used (to prevent the coagulation of a necessarily rather large amount of blood) and if there be assurance that no other infection is being transmitted by it, an aspect which must not of course be forgotten in collecting and preparing serum. Authorities differ as to the stability of the serum, but on the basis of English experience we may conclude that it can be filtered, treated with preservative and stored for considerable periods without losing its activity. Drying would probably preserve it indefinitely, although this method has apparently not yet been tried.

The ideal treatment of measles in a family where the day of exposure to infection can either be placed accurately or deliberately arranged is unquestionably to give convalescent serum on about the seventh day and thus secure a mild attack with subsequent permanent immunity. On the other hand, when children ill or debilitated from some other cause are exposed to infection, as may happen either in isolated instances or in the ward of a children's hospital, full protection should be afforded by serum given early. Opportunities for using this simple and valuable method of prophylaxis fall to the lot of almost everyone, and it is to be hoped that local authorities in many parts of the country may arrange for the collection of serum from suitable patients, more particularly in fever hospitals, and for its distribution.

The protective power of serum from the recovered subject is a feature peculiar to virus diseases; there is no bacterial infection in which any such striking effect can be obtained, and there are reasons for believing that the protective substance present in such serum differs in its properties and behaviour from any of the recognized bacterial antibodies. The action of such substances has been demonstrated experimentally in a large variety of virus infections and, clinically, in several infections besides measles. In none of these is the clinical evidence of its efficacy equally complete, a fact attributable in part to a difficulty in administering serum at an early stage, and in part to insufficient trial. In poliomyelitis the uses of convalescent serum deserve the fullest exploration: the results obtained in a recent outbreak in Australia are claimed to be satisfactory (MacNamara); success depends on recognizing the disease in the pre-paralytic stage. The results in chicken-pox and mumps are doubtful (Gunn). Encouraging results are reported in post-vaccinal encephalitis (Horder, Hekman), with the serum of a recently vaccinated subject. It is probable that the full possibilities of this method are by no means yet ascertained, and the advantages of using human instead of horse serum need hardly be emphasized.

Summary

A review of the progress of specific therapy during the past ten years calls attention to three important new methods of immunization, each depending upon a different principle. Inoculation with living, but attenuated, bacteria is represented in the use of B. C. G., a method still in the experimental stage, but offering at least some hope of immunization against tuberculosis. Inoculation with preparations of bacterial toxin has been shown to be capable of producing immunity to

diphtheria and scarlet fever. The injection of serum from recovered human cases can be used at will either to prevent or to attenuate an attack of measles, and possibly to modify the course of other infections.

Although these methods can be applied on a large scale only by the action of public health authorities, their employment in individual cases or in small communities remains to a large extent the duty of the individual practitioner, who may find in them the means of performing valuable service.

Recurrent Boils

By RUPERT HALLAM, M.D.

(Abstracted from the *British Medical Journal*,
October 8th, 1932, p. 670)

THERE is a singular disposition to regard the individual suffering from a boil with a certain degree of levity, yet we have it on no less authority than the Bible that 'Satan went forth from the presence of the Lord and smote Job with sore boils from the sole of his foot unto his crown'. Those who have endured the extreme pain of a boil in the external auditory meatus must indeed be tempted to suppose that the same master hand was responsible for their affliction.

To Pasteur is due the honour of demonstrating that the boil is caused by the action of the *Staphylococcus aureus*—a micro-organism which he found also in pus from carbuncles and osteomyelitis—but we are well aware that mere contact between the skin and this organism is not necessarily followed by the development of a boil or carbuncle. The number, the virulence of the cocci, and the degree of resistance of the individual are the determining factors, as in the case of many other infections. Some investigators hold that *Staphylococcus aureus* is not a normal habitant of the skin; others state that every man is a carrier of pyogenic cocci. Investigations of this nature must necessarily be incomplete, for it is impossible to include in the examination the whole skin surface or the contents of the follicles; neither is there at present a satisfactory means of distinguishing between virulent and non-virulent bacteria of the same species. We may, however, assume that most individuals, if not all, are frequent carriers of *Staphylococcus aureus*. The relative number will be influenced by such factors as personal cleanliness and occupation. The personnel of a hospital, for instance, must be constantly exposed to the infection. The age of greatest vigour is that most susceptible to the infection. The highest incidence is amongst males in the second, third and fourth decades of life.

Trauma is no doubt responsible to a certain extent for the selection of these decades. On the other hand, children during the school age are subjected to much trauma, yet the incidence at this age is low, while practical experience teaches us also that sedentary workers are frequently the victims.

The difference in environment and habits of the sexes is hardly sufficient to explain the sex incidence. It therefore appears that the female skin offers a less suitable habitat for the bacteria.

SOME CONTRIBUTORY CAUSES

Some observers maintain that the first boil is the result of an accidental infection, and that subsequent boils are merely consequent infection of the follicles. But boils are not a common complication of other pyogenic diseases, such as sycosis and chronic osteomyelitis, where the skin of the whole body is subject to constant contamination with the *Staphylococcus aureus*. Again, it is notable that persons suffering from furunculosis will often give a history of having had previous attacks of the condition, with intervals of a year or more between. This shows that their follicular resistance to the invasion of the staphylococcus is low. Unfortunately we know little of the immune biological character of the skin. It is true, we are aware, that boils and carbuncles are relatively frequent in diabetes,

yet glycosuria is met with in a very small percentage only of those suffering from furunculosis. An unusual partiality for sweets is sometimes admitted by the victims of the complaint, and a drastic reduction in the consumption of sugar is of great service in the treatment of many cases. A more important ætiological factor which has not received the attention it deserves is the frequent presence, in cases of recurrent boils, of an intercurrent infection on the skin. This occurred in 31 out of 98 consecutive cases examined from this point of view. Thus, 11 were found to be suffering from pruritus ani, 9 from scabies, 4 from impetigo, 2 from pediculosis corporis, 1 from otitis media, 1 from whitlow, 1 from abscess, 1 from oil acne, and 1 from *perléche*.

It is conceivable that any of these coexisting lesions may have been acting as a focus for the staphylococcal infection of the skin. Their recognition is therefore of obvious importance. Another fruitful source of folliculitis and boils is the application of fomentations to suppurating wounds of the skin, the furunculosis often persisting long after the original wound is healed. To avoid this complication it is advisable to restrict the wet dressings to the smallest dimensions. A half per cent. silver nitrate solution may be employed with advantage, for it does not have the tendency to produce a folliculitis of the surrounding skin.

Fortunately the sufferers from furunculosis are usually unaware of the complications which may assail them, yet there are probably more fatalities arising from it than from any other skin disease. At one institution with which I am associated there were, during 1931, four deaths which could undoubtedly be attributed to boils. Of these cases, a girl aged 17 and a man aged 47 succumbed to a boil on the upper lip, a boy aged 16 and a man aged 57 to a carbuncle on the neck. The face and neck are recognized as a danger zone, but, in addition, surgeons meet with perineal and prostatic abscess and osteomyelitis following one or more boils. Any prophylactic measures which may prevent further boils are therefore of very definite importance.

A reduction in carbohydrates is a matter of first importance. That the skin should be kept as dry as possible is a maxim which is supported both by clinical and by experimental evidence. The self-disinfecting power of the skin is influenced by the amount of moisture present. It has been found in experiments with *B. prodigiosus* that these organisms when applied to the skin diminished rapidly in number, particularly during the first ten minutes.

Similar results were obtained when cultures were placed on inert material, such as glass, paper, and hide. The rate of disappearance in all instances was governed almost directly by the amount of moisture present, and the experiments failed to indicate any inherent germicidal power of the skin. These findings are of the utmost importance in view of the fact that the fomentation still reigns supreme as a dressing for boils. Admittedly it is comforting, and also reduces the pain, but at the same time it cannot be too strongly emphasized that it is a common cause of the recurrence—the purulent discharge soaks into the dressing and staphylococci are spread to the neighbouring follicles, where they are encouraged to multiply under the optimum conditions of heat and moisture. My own practice is to recommend the frequent cleansing of the surrounding skin with spirit and the direct application of pads of gauze soaked in spirit as a covering to the boil.

Under the heading of prophylaxis must be considered the advisability of using such measures as vaccine therapy, chemotherapy, yeast, purgatives, etc. There is a wide divergence of opinion concerning these measures. For instance, Sabouraud states that staphylococcal vaccine, prepared according to his technique, rarely fails in subjects less than 50 years of age, and he concludes with the slogan, 'One can, and one must, vaccinate against furunculosis'. On the other hand, his fellow country-man, Clement Simon, holds the

opinion (with which I concur) that vaccines in recurrent boils do not live up to their reputation. Brocq was equally dogmatic in testifying to the virtues of fresh yeast for the malady, for he referred to it as a specific of the same value as mercury for syphilis and quinine for malaria. The yeast he employed may be different to the variety used by brewers in this country; certainly an extensive trial of the latter convinced me that it is useless for the purpose.

It is impossible to discuss the innumerable remedies which have been sponsored, but I feel that my remarks would be incomplete if I did not refer to colloidal manganese hydroxide. I have given it an extensive trial over many years, and I am convinced of its utility. As regards the local treatment, most writers refer to the possibility of averting a boil in its early follicular stage. Puncture with the galvano-cautery, injection of pure carbolic acid, and painting with iodine, each has its advocates, but although some favourable results may be obtained success is by no means the rule.

The treatment of the fully-developed boil is also a debatable subject. Whilst some advocate either excision or incision, others, more conservative in their ideas, allow Nature to take its own course. In either case it is the prophylactic measures taken to prevent reinfection of the skin which are of greater importance.

Common Maladies and Their Treatment Nasal Catarrh

By WM. STUART-LOW, F.R.C.S. (Eng.)

(From the *Prescriber*, November 1932, Vol. XXVI, p. 325)

THE medical mind is clearly made up on the matter of the causation of head colds, namely, that microbic organisms gain a lodgment in the nasal passages, directly or indirectly, being introduced by the finger, applied by the handkerchief, which is often very foul, and constantly inhaled from the respired air, especially in crowded railway carriages. The chief reason, therefore, for the prevalence of nasal catarrh is that ordinary precautions are seldom taken to avoid the spread of the trouble from person to person. So much, then, for the cause and the method of dissemination.

It is well known that many persons are constantly contracting colds in the head—indeed, they are hardly ever free, life being more or less a continuous misery—but it is not so well known that there is a definite reason for this state of affairs, that it is easily remediable, and that such persons are a constant danger to others—their friends in the office and the home, and their fellow-travellers in trains.

The chief cause of this susceptibility to nasal catarrh is an anatomically disturbed nasal interior, due in most cases to an injury sustained when young, sometimes even at birth, sometimes in the football field, frequently in the commonest accidents, such as falls. This explains why one or two members of a family are constantly contracting colds while the others escape; why some members of an office staff are always falling victims while others are immune.

An individual with a normal nasal interior, breathing even a not-too-pure atmosphere, is much less likely to become affected by nasal catarrh than another with a disturbed nasal interior breathing a purer air. To discover the cause of constantly recurring nasal catarrh it is therefore necessary that the nose should be skillfully examined, when some such disturbing factor as has been indicated will almost invariably be discovered. Until it is, and the cause has been eliminated, the person will go on contracting head colds to his own great discomfort and the jeopardy of everyone coming in contact with him.

It is not the person unvaccinated against colds who contracts and spreads nasal catarrh so much as the individual with the internal anatomy of his nose disturbed who is so vulnerable to nasal congestions. He is a veritable microbe generator, and a bacterial

disseminator in every coughing spasm and sneezing attack to which he is liable.

The inferior turbinal may be taken as criterion of a healthy nose, and it will be found to be a very correct standard to go by in the study of departures from the normal. The two entrances of the nose should be symmetrical and sufficiently patent to allow of a free ingress of air on both sides: this is of the greatest consequence, since any obstruction at the very entrance to the passages, such as collapse of the alar cartilages, or dislocation of the columellar cartilage into the entrance, by lessening the volume of the air current, directly leads to congestion and accumulation of discharge and so to nasal catarrh. If these seemingly simple and visible defects are not remedied, it avails but little to perform some skilful operation on the nasal interior for the removal of catarrh, as it will inevitably be a failure. The nasal septum should be straight; but it seldom is, although slight departures from the normal are of little consequence as a reason for the origin of catarrh. The inferior turbinals, easily visible on tilting the tip of the nose with the thumb, are normally rosy-red, rotund, resilient, and moist, and a free passage can be seen between their most prominent parts and the septum.

The commonest departures from the normal, as seen best in the inferior turbinals, consist either in exaggerations or the contrary of these healthy conditions. In chronic rhinitis the inferior turbinals are too rosy-red, too rotund, too resilient, secrete too much seromucous discharge, and the nasal passages are diminished and partially blocked, especially on lying down. In hypertrophic rhinitis the turbinal is enlarged but more firm in its consistency, less rosy-red and resilient, but nevertheless characterized by over-secretion. In atrophic rhinitis the turbinal is non-existent or very small, and is usually covered with septic crusts. The middle turbinal in the normal nose is usually easily seen on tilting the head a little backwards, and is rosy-red, uniform, smooth, and moist. The floor of the nose can be readily inspected from the front and is seen to be straight and concave, and should not contain any discharge. The nasal septum may be found more or less deviated to one or even both sides when there is a somewhat double deflection—to one side in front and to the opposite side farther back; or one or more spurs may be discovered projecting from one or both sides of the septum.

Two very common and yet often long undiscovered causes of chronic nasal catarrh are nasal polypi and involvement of the maxillary antrum. These may keep up a more or less constant nasal catarrh which baffles the physician's many efforts to remedy.

One of the commonest causes of a persistent nasal catarrh is the presence of mucous polypi in the nose. These are at first very small; they nearly always spring from the region of the middle turbinal, and hang free into the middle meatus. They also often start on the lips of the hiatus semi-lunaris, on the outer wall where the mucous membrane is rather loose and easily becomes congested and œdematous. The discharge is frequently of a watery character, and until the polypi cause blocking of the middle meatus this may be all that patients complain of, except that changes in the weather affect them—dry weather favourably, and wet unfavourably—as regards the amount of stoppage and discharge.

Nasal catarrh, generally with a fetor and a thick yellow discharge, is how nearly all patients suffering from chronic antral disease describe their complaint. On examination pus is seen on the floor of the nose and can generally also be detected running over the inferior turbinal and down under the middle turbinal. If this discharge is wiped away and the patient's head lowered and inclined to the opposite side for ten minutes so that the affected antrum is uppermost, on raising the head and again examining, pus is usually again to be found in these positions. Transillumination will show the maxillary antrum to be dark on the side

involved; and, if the inner wall of the antrum be punctured with a small trocar and cannula, pus can be blown and washed out, which, of course, is proof positive of septic antritis.

The treatment of nasal catarrh obviously depends upon the cause: it is therefore imperative to ascertain its source. Certain common rules apply to the treatment of all nasal discharges, and these should on no account be overlooked. It seems to be almost an instinct in the medical mind to start the treatment of nasal discharges by ordering syringing, and I am particularly desirous of giving warning against the danger of such measures. A sniffing nasal douche may be used, or a warm, soothing alkaline lotion might be sniffed into the nostrils from the palm of the hand with safety and advantage. Nothing more forcible than a gentle sniff of such a liquid into the nose is warrantable. Where the desire is only to clear and moisten the nasal passage, a prescription such as the following is good:—

Sodium chloride	45 grains
Sodium salicylate	45 "
Borax	90 "
Potassium chlorate	60 "
Glycerine	60 minims
Menthol water	to 6 fluid ounces

Of this mixture two teaspoonfuls should be added to two ounces of warm water and used to spray or sniff up the nostrils occasionally.

When fetor is present, a solution containing phenol, 1 grain, and sodium bicarbonate, 4 grains, in 1 fluid ounce of warm water is recommended. Sodium sulphate, 20 grains to the ounce, is also advantageous for dissolving away purulent discharge.

All lotions applied to the inside of the nose should be lukewarm; cold applications are never advisable. No irritating remedy should ever be used, as anything producing irritation rapidly induces congestion and obstruction by causing turgescence of the lining membrane.

In most cases of nasal catarrh after the discharge has been thinned, moistened, and partially removed by a suitable soothing lotion, the application of a soft ointment is very gratifying to the patient, as it protects any excoriated or abraded surface and prevents crusting of the discharge. No irritating constituent must ever be introduced into such ointment; individuals differ greatly in the sensitiveness of their nasal lining. It is always best, therefore, to begin with a very weak composition, such as 4 grains of menthol and 20 minims of oil of eucalyptus to one ounce of yellow soft paraffin. Two to four grains of cocaine (alkaloid) may be added should there be much congestion or sign of inflammation. Should the trouble lie in the middle turbinal region or above and behind it, an anterior nasal atomizer may be used. By this means the same ingredients, but in slightly stronger proportion and dissolved in liquid paraffin, may be made to reach the higher parts of the nose.

It is of supreme importance that these recurrent acute catarrhal attacks should be prevented, and certainly never be allowed to drag on or frequently recur. For, just as the parallel case of acute middle-ear catarrh, if not promptly treated by paracentesis, will lay the foundation of chronic suppuration of the middle-ear, so a neglected acute or chronic nasal catarrh frequently results in sinus infection, sometimes acute and sometimes chronic, thus establishing chronic nasal catarrh.

Hay fever is not by any means the best name that could be given to a condition which consists chiefly of a more or less sudden onset of watery nose-running with headache and sneezing—serous and sero-mucous nasal catarrh. Some persons are, undoubtedly, especially liable to nasal catarrh when grass-pollen dust is about, but the nasal interior, even in such persons, has been ready for the paroxysm, the lining membrane being chronically congested from the presence of some disturbance of its anterior anatomy, such as enlargements, deviations, spurs, polypi, or adhesions. Attacks often

cease after operation on such irregularities. This is the true explanation of so-called special susceptibility. Just as some people have very irritable skins, so some have a very sensitive nasal lining, and the inhalation of very little dust will bring about the symptoms commonly grouped under the name.

Those liable to acute nasal catarrh should frequent sea-side places when hay-making is going on; or, better still, if possible, take a sea voyage. In this way, by simply avoiding dust in any form in the inspired air, attacks may be prevented. A soothing application such as warm soft paraffin painted into and sniffed up the nostrils, thus coating the lining, will often prevent an onset; or, better still, plain liquid paraffin (light gravity) blown into the nose from an anterior nasal atomizer will ward off an acute rhinitis in the same way.

I have found useful the administration of phytin, containing as it does calcium and phosphorus which restore a want in the blood. It should be continued regularly for a few weeks. One-tenth of a grain of parathyroid is also helpful. Milk freely added to the diet, if otherwise advisable from a digestive point of view, is helpful in increasing blood-calcium. Anemia should be treated, and constipation suitably remedied. The blood-pressure is almost always too low—a blue congested nose, cold hands and feet, and complaint of feeling chilly being usual. In such aggravated cases I have found solution of adrenaline hydrochloride, 4 minims, three times a day, of the greatest assistance, even a few doses quickly restoring pressure equality, and giving a feeling of well-being and equanimity. This can be continued a few days at a time and will become a distinct help towards both treatment and prevention.

Locally the treatment of an attack must be essentially soothing, and after trying many different preparations I have resumed the use of cocaine: a warm 5 per cent.

aqueous solution of cocaine hydrochloride should be freely sprayed up the nostrils from a fine spray, and pledgets of cotton-wool soaked in the solution placed over and under the turbinates and left in position for five minutes. In persons specially susceptible to cocaine, 3 per cent. will suffice, and this alone will be enough to give relief after a few minutes. Should there be much diffuse turgescence of the lining, or even only patchy distribution of turgescence, it is best to use a cocaine solution mixed with equal parts of adrenaline solution and normal saline.

On the withdrawals of the plugs the inside of the nose should be carefully examined for departures from the normal, such as spurs, ridges, etc. In this way it may be ascertained whether these are likely exciting centres for the trouble, and if so, whether in the intervals of acute onsets these should be operated upon. Such congested locations so liable to sudden turgescence on even slight irritation from dust, cold air, etc., are suitable places for the application of the galvanocautery, but only when the acute attack has subsided.

The patient should have an anterior nasal atomizer containing plain liquid paraffin, and this should be freely used before going out in the air, as it acts as a protection to susceptible, sensitive mucous membrane. On no account should cocaine be ordered: it should be used only by the rhinologist and never given for the patient's own use.

The physician is often asked to say how head colds may be prevented, and he is sometimes reflected upon because his measures are futile. Patients, however, should be reminded that they must themselves fully and rightly carry out their part by trying to attain exemption. They must remember such simple measures as to keep warm, to shun crowded places, to get into their overcoats, and to keep their mouths shut when passing from heated rooms to the open air.

Reviews

A SHORT HISTORY OF BIOLOGY: A GENERAL INTRODUCTION TO THE STUDY OF LIVING THINGS.—By C. Singer. Oxford: At the Clarendon Press, 1931. Pp. xxxv plus 572, with 194 illustrations. Price, 18s.

MANY foolish things have been said by American millionaires and many of their statements, both foolish and wise, have received a considerable measure of publicity, but no one has achieved such heights in either foolishness or notoriety as Mr. Ford with his classical remark, 'History is bunk'. This same theme has been developed and satyriized by a brilliant English writer; he has painted a world for us in which all history has been banished, all books prior to a certain date destroyed; only the present and the future are considered of account. It is a safe world in which everything is ordered and nothing is left to chance. Specialisation has reached a degree of perfection. A man is not only trained from his infancy to fit him for one particular occupation all his life, but he is procreated (in a bottle) with that object. It is difficult to find flaws in this writer's argument, but one is supplied by the author of the book under review; he has shown how specialisation, if developed to its logical conclusion, must eventually lead to the death of scientific advance. The work by scientific specialists is so intricate and abstruse that it is often impossible for the general reader to understand it. It is not merely a matter of the use of technical expressions; it is impossible to convey the ideas in any language to a mind not specially trained to receive them. The process of learning more and more about less and less will continue until eventually no specialist will be able to understand the results of any other specialist's work; thus no specialist

will have a scientific heir and each specialist's life-work will die with him.

It is obvious that far more liaison between different scientific specialists is necessary. It is not very clear how this is to be brought about; many general scientific surveys have been written, but they are on the whole unsatisfactory. Charles Singer considers that the historical method of approach is most satisfactory. The book under review is his justification for this contention, and incidentally a complete refutation of Mr. Ford's dictum. He has traced the advance in biological knowledge from the times of Hippocrates and Aristotle to Galen, then over that amazing blank of a thousand years, the dark ages, to the times of the re-birth of scientific enquiry in the thirteenth century, through its early stages of slow advance which has gradually accelerated during the last six or seven hundred years until the rate of progress of knowledge has reached the alarming speed of the present day. The scientist of the six hundred years ago was a universal scientist, he knew something about everything that could be called scientific, and it is only during the last century or so that specialisation began to develop to produce the myopic scientist of the present day.

Written in a very pleasing style it is an extremely easy book to read. The author has managed to use language that anyone with an ordinary education can understand but which is not irritatingly kindergarten. It is a book that every 'specialist' should be compelled to keep in his library, and yet it is one that anybody could read again and again with pleasure and profit.

It is only necessary to add that the book is published by the Oxford University Press.

L. E. N.

MEDICINE: ESSENTIALS FOR PRACTITIONERS AND STUDENTS.—By G. E. Beaumont, M.A., D.M. (Oxon.), F.R.C.P., D.P.H. (Lond.). London: J. & A. Churchill, 1932. Pp. xvi plus 719, with 61 illustrations. Price, 21s.

DR. BEAUMONT'S book, *Essentials of Medicine*, has been eagerly awaited by those physicians who practice general medicine. The author, in collaboration with Professor Dodds, was responsible for *Recent Advances in Medicine*, which achieved such enviable notoriety and which, in its many editions, provided for years, a concise, clear and up-to-date account of modern medical work.

The present book is the outcome of five years labour and the result is a book of outstanding merit. It is a complete index of modern medicine in concise form. The attempt to serve both the student and practitioner is always fraught with difficulty, but we have nothing but praise for the manner in which Dr. Beaumont has carried out his difficult task.

The book is, in reality, a synopsis of medicine and there are few known medical conditions that do not receive mention. Each heading is followed by a short but up-to-date account of clinical findings and treatment. If one were inclined to criticise, one might say that the headings were too numerous, and the descriptions of the more important conditions and their treatment too sketchy. If however Dr. Beaumont had made his headings less numerous the book would have been incomplete; if he had made his descriptions more detailed it would have become too bulky. We think he has carried out a very difficult task, that is a complete survey of modern essential medicine, with consummate skill and ability and we have no doubt a copy will find its way into the library of every progressive physician.

We would especially pay tribute to the section on diseases of the nervous system. This section is a model of lucidity and is well provided with excellent plates of illustrations.

J. D. S.

MEDICINE: ANALYTICAL REVIEWS OF GENERAL MEDICINE, NEUROLOGY AND PEDIATRICS. September 1932, Vol. XI, No. 3. Baltimore, U. S. A.: The Williams and Wilkins Company. (English Agents are: Baillière, Tindall and Cox, London.) Price, 21s. per volume and postage 2s. 6d. Single copy: 6s. 9d.

THIS last number of *Medicine* is yet another useful publication which will be of great interest to members of the medical profession. It contains three extremely instructive articles; the first and the chief article deals with syphilitic optic atrophies; a subject regarding which our ideas are still in a very confused state. The author of the article has given a well-considered and critical digest of the whole medical literature on the subject and has offered his own conclusions and opinions on many clinical and pathological phenomena. The treatment aspect has received particular attention, various techniques of treatment being described. The rôle of arsphenamine, and other important anti-syphilitic remedies has been very thoroughly discussed. Arsphenamine intravenously, bismuth, mercury and the iodides, in any combination or for any length of time, have all been shown to be useless. Sub-dural treatment with arsphenaminized serum or neoarsphenamine injected intraspinally or intracranially are the treatments advocated. Fever therapy, chiefly with malaria, has been considered to be still in the experimental stage.

The second article represents the Harvey Lecture on experimental epidemiology by an expert in public health. The subject is rather abstruse, but will be very informative to those interested in the transmission problems of various bacterial and microbic diseases. The third article on factors concerned in the evacuation of the gall-bladder is particularly valuable to the

physiologists. It contains much useful data which will guide the clinicians in their treatment of jaundice and other obstructive manifestations of gall-bladder trouble. This journal should greatly appeal to the practitioners and those engaged in post-graduate study.

R. N. C.

INTERNATIONAL CLINICS.—Edited by H. W. Cattell, A.M., M.D. Vol. II, Forty-second Series. London: J. B. Lippincott Company, 1932. Pp. viii plus 307. Illustrated. Obtainable from Messrs. Butterworth & Co. (India), Ltd., Calcutta. Subscription Rs. 37-8 per year. Price, Rs. 9-6 per volume.

INTERNATIONAL clinics is a collection of a series of lectures on clinical and general medicine, surgery and other allied subjects. The book contains contributions from leading members of the medical profession throughout the world and is a very useful publication. The present volume belongs to the 42nd series and bears the high standard of the previous numbers. It consists of ten sections. The first deals with biochemistry and fully discusses the recent application of Claude Bernard's theory of anaesthesia. The second section deals with the surgical diagnosis, indications and safeguards for the operation of hernia, and dietary as a therapeutic measure. The author points out the importance of careful taking of history and physical examination in the diagnosis of disease, and emphasizes that radiography, microscopy, etc., should be only used as confirmatory aids. The sections on ulcerative endocarditis, recent progress in surgery, light-therapy and progress in paediatrics are lucid and brief, and will be of special interest to practitioners. The book is written in a simple and easy style, and forms very light reading, although it is full of information concerning the recent advances in the realms of medicine. At the end of each chapter a bibliography of interesting papers is given for those who want to have further information regarding different subjects. This volume will be very useful to senior students, practitioners, and to those taking up post-graduate work.

R. N. C.

'INTERNAL MEDICINE: ITS THEORY AND PRACTICE.'—Edited by John H. Musser, B.Sc., M.D., F.A.C.P. London: Henry Kimpton, 1932. Pp. xi plus 1316. Illustrated. Price, 50s.

THE addition of yet another book on medicine to the already large and overflowing library of books on the subject may appear superfluous to many readers. The book under review, however, is a little different from the ordinary textbook and presents several important features which will not fail to be noticed by careful students. The chapters are contributed by a group of twenty-seven authors—all teachers of repute in America, who can speak with authority on the subject. With the increasing length and complexity of the medical curriculum and the consequent need for specialisation in different branches of medicine, no one man can deal satisfactorily with the whole subject, and it is only proper that different sections should be entrusted to those possessing special knowledge in individual subjects.

All the chapters have been well written. Most of the chapters are preceded by a discussion of the general features common to the group of diseases dealt with in that section. This gives a wide outlook into the nature of the problem and is conducive to better and clearer understanding. The infectious diseases have been grouped under the various causative organisms and are not grouped together under the generic term of fever as is the case in many other books. The section dealing with the diseases of the blood is full of new terms and should specially interest the reader. The structure of the bone marrow and the mechanism of production of anaemia have, however, been meagrely dealt with. Avitaminosis, and pulmonary tuberculosis

are sections which are particularly well done. Like many other American books, it is not unwieldy. It is written in that racy, pleasant and readable style which characterises the American publications. The printing and format leave nothing to be desired.

R. N. C.

WHEELER AND JACK'S HANDBOOK OF MEDICINE.

—Revised by John Henderson, M.D., F.R.F.P.S. (Glas.). Ninth Edition. Edinburgh: E. & S. Livingstone, 1932. Pp. xix plus 654. Illustrated. Price, Rs. 9-6. Obtainable from Messrs. Butterworth and Co. (India), Ltd., Calcutta.

The original edition of this work appeared in 1894 and it is proof of its popularity that the book has now reached the ninth edition.

A handbook, as pointed out by the author, is not a textbook and cannot be expected to contain the same amount of substance. At the same time, it should have certain attributes peculiar to its own class. It must be a complete, concise, though naturally not exhaustive, review of the subject, assembled in a volume of such a size that it may be the constant companion of the student both at the bed-side and elsewhere. Further, as it is intended for the fledgeling, the subject-matter must be presented in predigested and assimilable form. In fulfilling these essentials, the author has been conspicuously successful, and there is no question but that the new edition will gather to itself a host of friends and that a large number of students will find it invaluable both at the outset of their careers and during the revision period before examinations.

In this book the author has exercised a rigid economy in words and space, but has amplified and made the text more clear by the inclusion of tables, both of diagnosis and classification, and of a number of instructive diagrams.

A valuable feature is to be found in the preface to each main subject giving not only a description of the relevant anatomy and physiology, but also a careful consideration of the signs and symptoms to be found at the bed-side, together with details of such laboratory methods as may be necessary.

Reviewers have from time to time in these pages advised that, in works of this size, the subject of diseases exclusively confined to the tropics should be left out. In this instance, we endorse that view. Not only is the space allotted too small to allow of the conveyance of any clear impression of the disease described, but also, in many instances, the opinions expressed are by no means in accordance with the experience of those who deal with such diseases at first hand: for example, we cannot regard puncture of the liver as a legitimate first step in the diagnosis of kala-azar, nor is gangrene of the nose a standard complication in cholera.

To turn to other matters, we might venture to appeal for a revision of the chapter on rheumatic fever, in the next edition. In the present chapter all mention of the equally important and insidious rheumatic infection of young children is confined to three lines. Further, we should like to see the section on chorea removed from its present surroundings and included in a chapter entitled 'rheumatic infections'.

F. H. V. H.

'TUBERCULOSIS OF THE LUNGS.'—By S. L. Piplani, B.Sc. (Hons.). London: John Bale, Sons and Danilesson, Ltd., 1932. Pp. 205. Illustrated. Price, 15s.

IN a preface, Mr. S. L. Piplani states that the object of writing this book is to give information to those who are suffering from, or are apprehensive of, pulmonary tuberculosis. While calling the book semi-popular, the author has dealt with such subjects as anatomy, physiology, embryology, and pathology. Obviously, such a book cannot be styled 'semi-popular'.

The book has been divided into two parts. The first part deals with the theory of pulmonary tuberculosis and it is doubtful if this part will interest very much the general reader for whom the book is primarily intended. The reader will not be interested to know that the volume of air in the lungs consists of tidal air, complementary air, and residual air, that tuberculosis in the parrot is caused by the bovine type of tubercle bacillus, or that the lungs grow from the fore part of the alimentary canal. What he would like to be told is the way in which infection takes place in the body, the symptoms he should look for, and the way he should live to get rid of the trouble.

The theory of immunity has been discussed rather elaborately and will not be of much use to the average reader. The author is under the wrong impression that in tuberculosis the percentage of lymphocytes is higher than usual. He is not aware of the recent work that has been done on leucocytic reactions in pulmonary tuberculosis which shows that the monocyte represents tubercle formation, the neutrophil represents tubercle undergoing abscess formation, and the lymphocyte represents the healing phase of the tuberculous lesion.

The second part of the book deals with treatment and will be of some interest to the reader. Morphine has been referred to by the author as an 'heroic' measure that is employed for 'obstinate and recurring cases' of hæmoptysis. Morphine has no direct action on hæmoptysis; it helps indirectly by giving mental rest to the patient which is no less important than physical rest, and it also allays unnecessary cough. Morphine is never intended to be given as a 'cure' for hæmoptysis.

A long chapter has been devoted to the function and use of tuberculin. Tuberculin has been given extensive trial and found wanting. Its use in treatment on any large scale is not in evidence anywhere now—not even in its home, Germany.

In the chapter on Sanocrysin and allied products, the author has unnecessarily gone out of his way to criticise the Ayurvedic system of medicine as being unscientific and based on empiricism.

Treatment by artificial pneumothorax was suggested for the first time in 1822 by James Carson of Liverpool, and not by Forlani and Murphy who were not Englishmen as the author seems to believe. The results obtained from thoracoplasty are far from discouraging as the author says when it is remembered that the operation is performed in cases who have failed to improve under other methods of treatment and have been given up as hopeless.

There are many inaccuracies in the book which has been made too technical to be of much use to the popular reader. It contains a collection of case results drawn from various sources and a number of illustrative diagrams. We did not observe many misprints in the book, but surely when the author refers to a sanatorium at 'Bhaoli' he must mean 'Bhowali'.

Y. G. S.

SYNOPSIS OF THE BRITISH PHARMACOPOEIA, 1932.—By H. W. Gadd. Twelfth Edition. London: Baillière, Tindall and Cox, 1932. Pp. viii plus 162. Price, 3s. 6d.

THE publication of a new pharmacopoeia is a matter of considerable importance to all who are engaged in the profession and trade of healing. A new British Pharmacopoeia was published in 1932.

A pharmacopoeia is primarily a means of providing a basis of understanding between the physician who prescribes and the pharmacist who dispenses the medicine, so that when any medicine is prescribed by name the dispenser will know exactly what is required. In the new pharmacopoeia a number of changes have been made; when a physician is prescribing, it is of importance that he should be fully aware of these changes, as unless he specifies 'old pharmacopoeia' on his prescription the dispenser will almost certainly make

it up on the new standards, and his patient will not be getting the exact medicine he wished him to get. For this reason it is very important that all concerned should acquaint themselves with the new work on the earliest possible occasion. For the busy practitioner this is rather a formidable task. Furthermore, he cannot carry with him the large volume of the new pharmacopœia, but he will find that this synopsis will fit into the smallest of waistcoat pockets, without appreciably distorting the most tight-fitting of coats.

The synopsis gives a full list of the drugs now included in the new pharmacopœia, with the dose, both in the imperial and in the metric systems, a few words on the characters of each drug, and a few more words of detail in the 'remarks' column. These details will be found quite sufficient for any prescriber.

There is in addition a separate list of new drugs which were not included in the old pharmacopœia, another list of drugs which appeared in the old pharmacopœia but are not in the new one, a list of drugs whose names have been altered, and, finally, a list of those whose composition has been altered. A comparison of the lengths of these lists is of interest; the new preparations, amongst which we notice 'totaquina', fill four columns, whereas the exclusions fill eleven columns. (It is very encouraging to think that the medical student will gain a little relief in this direction from his ever-increasing burden.) The list of altered names fills $3\frac{1}{2}$ double columns whereas the drugs of altered composition fill only just over one column. Amongst the 'axed', many of us will see old friends departing; all the decocta and all the vina have gone, and the unguenta seem to have suffered heavy losses.

There is much other valuable information in this minute volume.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Twentieth Edition. Volume I. By W. H. Martindale, Ph.D., Ph.Ch., F.C.S. London: H. W. Lewis and Co., Ltd., 1932. Pp. xlviii plus 1216. Price, 27s. 6d.

THE first volume of the twentieth edition of the extra pharmacopœia has just been published. The book is so well known that it scarcely requires any special introduction to members of the medical and pharmaceutical profession. It was first published in 1883, just 50 years ago and has ever since held a most unique and privileged position in the medical and pharmaceutical libraries. The progress of medical chemistry and pharmacology has been phenomenal since the first edition was written and the pages have had to be frequently revised, rewritten and added to. The first volume contained only 313 pages. Since 1912 the subject-matter has grown to such an extent that it was thought desirable to divide it into 2 distinct volumes. The first volume of the twentieth edition alone contains 1215 pages excluding the introductory pages and the second volume is expected to have another 800 pages. This in itself shows that the book has kept itself abreast of the modern advances. The original scheme has, however, been largely retained and those who used to refer to the old volumes constantly will not find it difficult to find what they want at a glance. Though the edition has come out practically simultaneously with the new British Pharmacopœia, all the changes therein have been fully incorporated and a synopsis of the alterations, in tabular form, has been appended. Apart from the valuable references to the original papers with regard to various drugs and chemicals, the pharmacists and the drug-store proprietors will find the various laws and regulations for keeping, dispensing and selling poisons of great use to them. The Therapeutic Substances Act with the latest regulations published in 1931 is also given. The book is one without which no medical library can afford to carry on.

R. N. C.

AIDS TO SURGICAL DIAGNOSIS.—By C. P. G. Wakoley, F.R.C.S. (Eng.), F.R.S. (Edin.). Second Edition. London: Baillière, Tindall and Cox, 1932. Pp. vii plus 172, with 6 figures in text. Price, 3s. 6d.

THIS book is in the well-known students' 'Aid' series. It is very concisely written without waste of words. Points of importance are duly emphasised and easy of reference. It should prove of great value to the medical student and also to the busy practitioner.

A. H. P.

A SHORTER SURGERY, Third Edition. A Practical Manual for Senior Students.—By R. J. McNeill Love, M.B., M.S. (Lond.), F.R.C.S. (Eng.). London: H. K. Lewis & Co., Ltd., 1932. Pp. viii plus 414, with 96 illustrations. Price, 16s.

THIS book has been written for the medical student and the more important principles of surgery have been condensed and crystallised as much as possible. No attempt has been made to cover the whole field of surgery, but only that aspect of it which is necessary for qualification examinations.

The various diseases and surgical conditions are rigidly classified, but sometimes rather at the expense of pathological accuracy. The whole subject of burns is dealt with in one page in the chapter devoted to surgical pathology, although the pathology of burns is not discussed.

Infections of the fingers and hand are not mentioned, yet two whole pages of small type are devoted to Spiller's operation for section of the antero-lateral tracts of the cord. This with a number of other operations which are described in detail has surely no place in a *shorter surgery*.

On the whole however the matter is sound and concise. The illustrations are good and appear in most instances in close relation to their appropriate text.

Students will certainly obtain much useful information and help from this book, provided it is read in conjunction with, and not instead of, their surgical textbooks.

A. H. P.

INTRACRANIAL SUPPURATION.—By E. M. Atkinson, M.B., B.S. (Lond.), F.R.C.S. (Eng.). London: Jonathan Cape, 1932. Pp. 127. Price, 5s. Obtainable from Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 3-12.

'INTRACRANIAL Suppuration' is one of the Modern Treatment Series. It is a small volume of 124 pages. There are six sections—general pathology, prevention of intracranial complications, osteomyelitis and extradural abscess, infective thrombosis of the venous sinuses, meningitis, and brain abscess. The author remarks in the preface that it has not been an easy book to write. He has, however, admirably succeeded in bringing a vast amount of scattered work within the compass of this small volume.

The chapters on infective thrombosis and brain abscess are particularly good. In the latter, the desirability of operating without waiting for localising signs is emphasised. The style is simple—almost conversational in places—and the subject is clear and eminently practical. The book is extremely handy and the printing excellent.

S. A. McS.

'THE PRINCIPLES AND PRACTICE OF OTOTOLOGY.'—By F. W. Watkin-Thomas, F.R.C.S., B.Ch. (Camb.), and A. L. Yates, M.C., M.D. (Lond.), F.R.C.S. (Edin.). London: H. K. Lewis and Co., Ltd., 1932. Pp. xli plus 568, with 199 (5 coloured illustrations). Price, 25s.

THIS new volume on a specialised subject will appeal to its intended readers—the young doctor taken to the D. L. O. or other higher degrees, and the general practitioner surgeon.

It is well written and the numerous illustrations and line drawings are clean and well reproduced.

The authors have drawn on a wide field for the contained material and have given a clear, well-balanced and up-to-date account of the subject. There are copious, easily-accessible and recent references throughout the book, which add greatly to its value.

F. H. B. N.

'DISEASES OF THE NOSE, THROAT AND EAR.'

By A. L. Turner, M.D., LL.D., F.R.C.S.E. Third Edition. Bristol: John Wright and Sons, Ltd., 1932. Pp. xxvi plus 465, with 250 illustrations in the text and 19 plates, of which 8 are in colour. Price, 20s.

THIS excellent book requires no recommendation. Written in clear style and based on the sound and conservative teaching of the Edinburgh school, it should be in the hands of every practising medical man. For the student it is a trustworthy guide and to the practitioner a tried and proved friend.

Much new matter and many new illustrations have been added in this edition, bringing it thoroughly up to date, without unduly enlarging the size of the book or increasing the price.

The editor, collaborators and the publishers are to be heartily congratulated on their production.

F. H. B. N.

'SOUND CONDUCTION AND HEARING.'

By A. Zund-Burguet. Translated by MacLeod Yearsley, F.R.C.S. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. 139. Price, 8s.

ENGLISH-SPEAKING otologists owe McLeod Yearsley a profound debt of gratitude for his scholarly translation of Mr. Zund Burguet's book. This volume should do much to popularise his electrophonoid method of re-education for deaf ears and to dispel a considerable voice of criticism against this method of treatment which has brought back hearing to so many sufferers.

We can recommend it to all, supporters and sceptics alike.

F. H. B. N.

A RADIOLOGICAL STUDY OF THE PARA-SINUSES AND MASTOIDS.

By A. Granger, K.C.B., K.C.I., M.D., F.A.C.R. London: Henry Kimpton, 1932. Pp. 186. Illustrated with 113 engravings. Price, 25s. net.

THE name of Granger in x-ray examinations of the nasal sinuses is one to be conjured with, and this little work is the outcome of the research work which he has brought to a successful conclusion in this field of x-ray investigation.

The book is essentially a collection of articles which he has written on the subject illustrated by reproductions of his private exhibits of radiographs at the Charity Hospital of Louisiana. They include experimental and comparative studies of the sinuses which are of the utmost interest and value to radiologists all over the world.

The reproductions of radiograms are on the whole clear and show with sufficient distinctness the radiological appearances of the pathological conditions involved. If one were to make a criticism, it is to be noted that the pictures have been produced without the aid of a grid, which as we know, greatly adds to the clearness and contrast. The Potter-Bucky diaphragm of course is the best of these aids to radiography and the writer has designed apparatus whereby a Potter-Bucky grid can be readily used in any of the desired positions. A fixed grid of the Lissom-type could of course be fitted to any of the apparatus described. The absence of grid technique has undoubtedly affected the clearness of the reproductions; but the value of the angular positions described remains firmly established.

We have nothing but praise for the general get up of the volume. It is worthy of the best traditions of such a distinguished firm of publishers.

J. S. S.

THE LEGAL AND ETHICAL ASPECTS OF MEDICAL QUACKERY.—By L. M. Minty, Ph.D., B.Sc., B.Com., LL.B. London: William Heinemann (Medical Books), Ltd., 1932. Pp. xviii plus 262. Price, 7s. 6d.

THE writer of this book is not a medical man; the book has suffered a little on this account. On the other hand it could not have been written by a medical man, unless he had had a vast amount of legal experience. The ideal book would be a collaboration between a medical man and a lawyer; the author of this book sought a medical collaborator but he was advised that the General Medical Council would be likely to disapprove. On the whole we feel that, if the addition of a medical collaborator would have affected the freedom of the discussion, it is after all as well that this collaboration was not brought about. There are many difficulties in the way of achieving the ideal.

The title of the book might well have been abbreviated, as it is almost entirely the legal aspects of medical quackery that are discussed. The author starts by giving a definition of the word 'Quack'. The exact meaning of the word has a very important legal significance and in one case a reversal of a £1,000 judgement was obtained because the judge had told the jury that to call a man a 'quack' meant that he was unqualified; its actual meaning is 'one who adopts the practices of a person who has no medical skill but induces patients to come to him by advertisement, self-praise and the abuse of others'. There are unfortunately qualified medical men who do adopt these methods, but it will be seen from this book that it is a very dangerous thing to call any man a quack in public, and though you may be exposing an arrant rogue and doing a signal service to your fellows, it will cost you a small fortune in legal fees, even if you do eventually obtain judgement in your own favour.

In the section on infamous conduct in a professional sense, the author shows himself prejudiced. It is in some ways a pity that he did not confine himself to citing cases on which he was not personally involved. He could then have given a less prejudiced criticism of the General Medical Council. He complains that the Act of 1858 gave the General Medical Council powers which the legislature never meant them to have. It strikes us as rather amusing that the medical profession should have beaten the legal profession on the latter's own ground. He considers that a new medical Act is necessary to make the General Medical Council treat all, famous surgeons and poor practitioners, alike. This accusation of favouring the rich is again a little unfair—the General Medical Council are notoriously lenient to knighted surgeons in their dotage, not, we are sure, because they are afraid of them but because on the whole they do little harm and would gain considerable notoriety by any legal action.

In the section on abortion the author is again, in our opinion, unjust. The injustice in this case is to this country and is born of ignorance. He implies that a considerable number of Indian students in England supplement their allowances by practising abortion. He writes, 'In India abortion is not an offence. The ordinary means used by the Dhahs or Indian professional abortifacient is to insert a twig.....'

Amongst the causes of death associated with the illegal operation of the abortifacient, he includes 'fright', *per se*, prior to the operation, not, we imagine, a common cause of death in an otherwise healthy woman.

The book is not very light reading and there is little comic relief; however, there was one sentence which amused the reviewer:—A member of the House of Lords protested violently against Lister being raised to the peerage, because a month previously for a fee of five guineas he had carried out a digital examination of this noble Marquis's rectum.

For the book as a whole and for the author's method of dealing with the various subjects we have nothing but praise to offer. Any medical man will find much that he

can apply in his own experience and he may find guidance for the future. To those who have a special interest in the legal aspect of medical practice the book will be very valuable indeed.

L. E. N.

A TEXTBOOK OF PATHOLOGY: AN INTRODUCTION TO MEDICINE.—By W. Boyd, M.D., F.R.C.P. (Ed.), F.R.C.P. (Lond.), Dipl. Psych., F.R.C.S., London: Henry Kimpton, 1932. Pp. 946. Illustrated with 287 engravings and coloured plates. Price, 45s.

As the author of this excellent book points out in his preface, in the matter of writing books on pathology it is not possible to serve two masters. A decision has to be made and in this case the author has decided—no doubt with the urging of the publishers—in favour of maummon, and has written this book for the benefit of the student, but his definition of the student is a comprehensive one, and his motto is apparently 'aren't we all'. The Gods he refers to such books as the fourteen-volume system of Henke and Lubarsch.

The author seems to regret that the student has to commence his studies in pathology before he has had any clinical experience and that he is therefore often unable to appreciate the significance of the pathological changes he is shown. To get over this difficulty the author has included a very short account of the etiology and clinical picture in many instances and in others he has given a valuable paragraph on the correlation of the signs and symptoms of the disease and the morbid changes as observed in the pathological laboratory. (We might mention, parenthetically, that clinical teachers complain that, when they commence their practical work, students have not sufficient grounding in pathology to enable them to appreciate the significance of clinical signs and symptoms. The only way to please both would be for a student, after having passed his final examination in all subjects, to go back to the beginning and take his whole course again; this is unfortunately not practicable in our temporal world.) The author has also realized the importance of the application of physiology and has in every case given a short résumé of the important physiological functions of the various organs.

The book is divided into the usual two sections, general and special. It is surprising what an enormous field has to be covered by a book of this nature and how little space can be given to each subject. The author has, however, made the best use of this space and has not 'sacrificed the student to satisfy his own sense of completeness'. This last sentence is paraphrased from the author's preface, but the words are almost those we used recently about another book, without the negative.

The author's style and method of presentation of the subject make the book easy and pleasant to read, but he introduces now and then remarks which the student might accept as aphorisms, and which do not deserve this appellation as they frequently require both amplification and modification. For example, while discussing hepato-splenic fibrosis, he writes 'when the liver is principally affected the condition is called cirrhosis. When the main lesions are in the spleen the condition is called splenic anæmia'. He also uses modern expressions which are occasionally so apt that even the most pedantic reader will forgive him, but the forgiveness is dependent on the aptitude, which is not always evident; reference to red blood cells being 'parked' in the spleen to meet an emergency cannot be forgiven on these grounds. The offending word comes in a paragraph commencing '*The bank function*' (of the spleen). Why exchange a good metaphor for a bad one?

These are, of course, quibbles which do not detract from the solid value of the book. We strongly recommend it both to the young student and to the practitioner.

L. E. N.

A NEW DICTIONARY FOR NURSES.—Compiled by Lois Oakes, S.R.N., D.N. (Lond. and Leeds). Edinburgh: E. & S. Livingstone, 1932. Pp. xvii plus 345. Illustrated. Price, Rs. 2-4. Obtainable from Messrs. Butterworth and Co. (India), Ltd., Calcutta.

There are possibly other dictionaries of this kind on the market but we have not seen them. The medical dictionary is too bulky and too expensive for the ordinary nurse, and in standard dictionaries many words in common use in the ward and operating theatre will not be found.

Despite the fact that much has been compressed into a very small space, the compiler of this dictionary has not been content to give the meaning of words alone, but has added notes which will be useful to a nurse; for example under 'avertin', in a column and a half the author has given most of the details necessary for making avertin solution, for preparing the patient, and for the administration of this drug.

A few pages are devoted to useful information on such subjects as abbreviations, comparative temperature scales, and weights and measures. There is an appendix which also contains useful information—e.g., a synonymy of diseases, dietary tables and calorific values—and a table of historical medical facts, which seems somewhat out of place in a book of this utility.

The book is well-printed and neatly bound, and is entirely suitable for the purpose for which it was compiled.

Annual Reports

REPORT ON THE SESSION OF THE OFFICE INTERNATIONAL D'HYGIENE PUBLIQUE, HELD IN PARIS FROM 25TH APRIL TO 4TH MAY, 1932. BY MAJOR-GENERAL J. W. D. MEGAW, C.I.E., K.R.P., I.M.S., DELEGATE FOR THE GOVERNMENT OF INDIA. SIMLA: GOVERNMENT OF INDIA PRESS.

The Office International d'Hygiène Publique is the headquarters and representative body of the signatory nations to the International Sanitary Convention. It holds meetings twice a year, and issues a monthly bulletin. Its proceedings and publications are in French and therefore may not obtain the publicity in India which their importance deserves. General Megaw's interesting summary deals with the spring meeting at which several matters were dealt with of extreme interest and importance to India. Perhaps the most important

is the question of the new Aerial Traffic Convention, and that part of it which particularly refers to the powers proposed to be granted to countries that have reasons to fear the introduction of yellow fever into their territories. India is in this position and should either the virus or a case of yellow fever be brought to India, the possibilities would be disastrous. The former contingency has been dealt with by legal powers, but the second remains a very real possibility. The convention previously proposed and agreed to by the 'Office' placed reliance on vigorous action at the ports of departure of the yellow fever country and at the ports of arrival of the defending country. The Government of India did not consider that these provisions afforded adequate protection and General Megaw was able to ensure such modification of the convention that the Government of India would have the right to refuse

or prohibit the landing of aeroplanes from yellow fever countries, if it thought it necessary to do so. When one considers the ease with which the yellow fever virus can be passed on to man even without the intervention of the mosquito, and the proved fact that the stegomyia can be transported easily by aeroplanes, the wisdom of such a provision of protection to India is manifest, and General Megaw is to be congratulated on the tactful manner in which he successfully removed misunderstandings and attained his object.

A great deal of attention was given to plague and its prevention by inoculation. Considerable doubt has recently been cast on the value of prophylaxis of plague by inoculation, especially by Italian and Dutch delegates. A report from India by Naidu and Taylor received close consideration and apparently convinced most of the assembly that prophylaxis by plague-vaccine, as prepared in the Haffkine Institute by carefully controlled methods at every stage, was a demonstrated fact, and that the Haffkine method of preparation by growth in broth was superior to the method by growth on a solid medium. Independent observation by Professor Ledingham appears to corroborate this statement. The new serum therapy of plague as reported by Naidu and Mackie also attracted attention. Reference is also made to important contributions by Williams and others on methods of rat destruction. These papers are published in the monthly Bulletin which should be consulted. Rat destruction and rat proofing of houses and ships are now recognised as measures of the first importance in preventing the carriage and propagation of human plague.

There are some interesting observations on smallpox and vaccination. Dried vaccine lymph has been exclusively used in French Equatorial Africa since 1924. It is apparently more easily transported than glycerinated lymph. Three cases of encephalitis following anti-typhoid inoculation were reported and a protozoon related to *Encephalitozoon cuniculi* of the hare has been reported to have been found by Dr. Kling in the neuraxons of two cases of post-vaccinal encephalitis.

Tuberculosis was also a subject of debate and an interesting note is given of a visit paid to Dr. Calmette's laboratory in the Pasteur Institute of Paris. Dr. Wefring of Norway holds that a negative von Pirquet reaction in nurses and others, who have to look after cases of tuberculosis, is a sign of dangerous susceptibility and that such persons should be inoculated subcutaneously with B. C. G. so as to give a positive von Pirquet, which would then denote a degree of protection. English public-health and tuberculosis workers have been accused of a want of enthusiasm in not experimenting with the B. C. G., but Sir G. Buchanan explained that the method of administration of B. C. G. to newly born infants, which also necessitates the removal of infants from infectious surroundings for a period of 4 weeks, would be impracticable in England and also unnecessary, since the measures in England have reduced the mortality amongst infants of under 1 year from 1,311 in 1921 to 585 in 1930. He admits that subcutaneous inoculation of B. C. G. would have an application in creating temporary immunity among persons who are not already immune, for example nurses working in tuberculosis hospitals or persons coming to towns from isolated rural areas.

The prevention of measles by immune serum, cerebro-spinal meningitis and psittacosis, relapsing fever, and the 'Bornholm' disease (acute epidemic myositis) which resembles dengue, were also discussed. The bacteriology of cholera is the subject of a short note in which the characteristics of the El Tor vibrio and the transformation of the agglutinable vibrio by bacteriophage into a non-agglutinable vibrio are discussed.

It will thus be seen that the subjects discussed in the Office are always of practical importance and General Megaw is to be thanked for his very interesting résumé of the April-May meeting. (We note that

extracts from the Bulletin of the Office are now being translated in the *Bulletin of Hygiene*.)

REPORT OF THE HEALTH OFFICER OF CALCUTTA FOR 1930. BY T. N. MAJUMDAR, D.P.H., D.T.M., F.C.S. (LOND.), F.R.S. (EDIN.). CALCUTTA: PRINTED AT THE CORPORATION PRESS. 1932.

It is a pity that the Health Officer of Calcutta Corporation has not been able to catch up the arrears of his annual reports. The year 1930 is a long time ago and some more up-to-date and timely information on Calcutta would be welcome. The report follows the usual lines and there is not much of novelty to record. Nevertheless the report is interesting. The 1921 population of 1,077,264 was still being used for purposes of calculation. The birth rate was 21.9 per 1,000, the death rate 28.9 per 1,000 and the infantile mortality 262 per 1,000 live births. Cholera caused 1,755 deaths (1.6 per 1,000), smallpox 1,818 deaths (1.7 per 1,000), tuberculosis 2,756 (2.5 per 1,000), deaths from malaria were reported to be 714 (0.66 per 1,000), typhoid fever deaths were 727 (0.67 per 1,000); kala-azar accounted for 315 deaths (0.29 per 1,000) and there were no deaths from plague. The features of the report are the comparatively low birth rate, the high infantile mortality, the high mortality from tuberculosis, and the comparatively high incidence of cholera and smallpox. Mortality from tuberculosis and cholera is a measure of the primary environmental conditions of housing, drinking-water and excretal disposal, and the evidence points to these matters being extremely defective in Calcutta. There seems to be no concerted policy in Calcutta in the matter of improving proper water-borne latrines and of providing an adequate supply of filtered water in the places where it is more urgently required. The Calcutta Improvement Trust is tackling the housing problem in a certain way, though only a fringe of it can be thus touched.

There are several interesting charts showing the seasonal variations in general mortality and in the mortality from cholera, tuberculosis, smallpox and fevers. There has been a reduction of recorded mortality due to malaria since 1922, but the present report does not touch on the recent happenings as regards malaria in the city. The report describes the work of the sanitary staff throughout the year and details the medical and maternity relief afforded through dispensaries and maternity homes.

The chapter giving the work of the Corporation laboratory contains some interesting reports of investigations on water and food analysis and there are also notes on algae in Calcutta water by Dr. Banerjee, Dr. Biswas and Dr. T. K. Ghosh which are worth reading. It is suggested that a sheet of copper should be placed in the front and sides of the weir at the 'thermocline' layer. So far as we know this has not been tried. Mr. Banerjee states that the modern 'catadyn' process was known to the ancient Indians as endorsed in the Smritis and the Puranas. The investigation of the algal problem in the complete manner suggested by Mr. Biswas would be valuable—we hope to see in the reports for 1931 and 1932 that some definite methods of inquiry have been started.

ANNUAL REPORT OF THE EXECUTIVE HEALTH OFFICER FOR BOMBAY FOR THE YEAR 1931. BOMBAY: THE TIMES OF INDIA PRESS, 1932.

The population of the city of Bombay at the census of 1931 was 1,161,383, which is a reduction of 14,531, or 1.23 per cent. during the decade of 1921–30, as compared with an increase of 20 per cent. during the decennium 1911–20. The reduction was really due to depression of trade conditions during the census-taking period and cannot be taken as a real average representation of the population changes during the last decade.

In vital statistics the noteworthy feature was the fact that for the first time since 1866, the number of births in the city was higher than the number of deaths.

The birth rate for 1931 was 23.4 per 1,000, and the crude death rate 21.6 per 1,000. The chief epidemic diseases, cholera, plague and smallpox, contributed only 80, 24, and 31 deaths respectively—not a large number.

Respiratory diseases are the chief cause of mortality, diseases of infancy coming next. Malaria along with ague and remittent fever take the third place (if 'old age' be excepted), while tuberculosis comes next.

Environmental conditions.—The water supply comes from Lake Tansa and is plentiful. It is not filtered but chlorinated.

Excretal disposal has several unsatisfactory features which require immediate improvement. The sewage outfall problem seems still to be undecided but no indication of the present stage of the discussion is given. Until this outfall question has been decided, urgent work on the sewage extension cannot be commenced. There are still over 13,000 basket privies causing terribly unsanitary conditions. The conversion of these proceeds gradually but is held up on account of the absence or insufficient capacity of the sewerage system in many localities.

Defective and insufficient housing of the working classes is still a feature of Bombay and no doubt accounts for the very high mortality from respiratory diseases. The City Improvement Trust has since 1898 provided 48,987 new tenements as against 33,535 tenements demolished. Financial considerations however are stated to have led to delay in taking action in a number of the areas which have been marked down as requiring attention.

In the matter of the protection of maternal and infant life, in the provision of accommodation of infectious diseases, and for the treatment of venereal disease and in the campaign against tuberculosis, Bombay seems to be far ahead of any other Indian city.

There are now 5 municipal maternity homes, in which 3,346 women were confined during 1931. Out of 29,336 births, 18,237 or 62 per cent. took place either in maternity or municipal and other hospitals. Puerperal sepsis accounted for 93 maternal deaths out of 198.

The infantile mortality rate was 272, being the lowest figure ever recorded in the city. Maternal benefits are now extended to women of the labouring classes. Municipal nurses and welfare centres provide means of educating and helping and advising mothers, and the Infant Welfare Society has 7 centres, two maternity homes and a crèche. No mention is made of voluntary welfare work in the city mills.

The chapter on malaria is interesting in view of Major Covell's *Report on Bombay Malaria* in 1928 and his *Report on Malaria in Calcutta* in 1931. Every endeavour is apparently being made to carry out Covell's recommendations with regard to the closure and protection of wells, cisterns, tanks and mill-ponds, etc. 131 deaths were registered from malaria but 1,398 deaths as due to ague and remittent fever. The last no doubt contains many deaths due to various non-malarious fevers. Inspectors still report a large amount of anopheline breeding, though the spleen rate in the districts reported as high by Covell appear to be coming down. There is a definite objection on the part of religious bodies to whole-hearted attempts to close wells and compromises have had to be effected. Spleen rates of between 12 and 20 are common still in the municipal schools. The summary of work done in 1931 in inspections and oiling, and mosquito proofing is impressive.

The impression one gets from reading the report is that the Health Officer and his staff are active, energetic and alive to the routine and special needs of the city. The primary matters of sewage disposal and housing seem to be hanging fire and should now be dealt with definitely and vigorously.

SIXTY-FOURTH ANNUAL REPORT OF THE DIRECTOR OF PUBLIC HEALTH OF THE UNITED PROVINCES OF AGRA AND OUDH FOR THE YEAR 1931. ALLAHABAD: THE SUPERINTENDENT, PRINTING AND STATIONERY, UNITED PROVINCES, 1932. PRICE, RS. 3.

Owing to financial conditions, no maps or diagrams are included in this year's report and the size of the report has been reduced by one-third. The essential statistical information and descriptive matter however have been retained and the report as usual is interesting reading. We understood that Colonel Dunn's tenure of the appointment as Director of Public Health comes to an end this year and those who have watched the progress of public health in the U. P. know how much advance has been made in the last 15 years, and that this has been due in very great measure to Colonel Dunn's energy, perspicacity, and imagination, and no less to his eloquence and persuasive powers.

The population of the U. P. in the decade 1921—31 increased from 45,375,787 to 48,408,763. An interesting table gives the birth and death rates of 1931 for the provinces of India and the rates of natural increase. Bengal has the lowest natural rate of increase 5.57 per 1,000, the Punjab's rate for 1931 being 16.75; that of the U. P. was 8.63.

The birth rate of the U. P. for 1931 was 35.6 and the death rate 26.97 per 1,000 and the infantile death rate per 1,000 births, 179.07. The figures of mortality for various diseases showed in general a decrease as compared with 1931. *Cholera* accounted for 31,118 deaths, *plague* for 31,225 deaths and *smallpox* for 3,385. *Fevers* claimed 1,075,281 deaths, a very high figure, of which 932,796 are attributed to malaria. This is a very high figure, but the records are stated not to be very reliable.

Tuberculosis gave a general death rate in towns of 1.34 and 1.85 in the larger towns. Under *respiratory diseases* were returned 36,612 deaths.

The elementary sanitation of the towns of the province does not seem to be of a very high standard and the fly and mosquito nuisances are widespread. Municipalities seem to be averse to act on the sanitary advice tendered, or on the lines laid down in the Municipal Manual. In the rural districts, the extension of the district health staff has been postponed for lack of funds. A good deal of work has been done in village uplift and rural reconstruction by committees. The Junior Red Cross work has caught on and would appear to be doing excellent service in the schools.

The special malaria branch continued its activities in various parts of the province. Perhaps the most interesting line of work is the attempt made to control malaria by the distribution of quinine and plasmochin; 20 grains of quinine and 1/6 grain of plasmochin are given for 3 days. The results are reported to be much better than with quinine alone. Similar treatment (21 grains of quinine and 1/2 grain of plasmochin daily for 3 days) were given in some of the jails. The relapse rate is reported to be much less than with quinine treatment and much less expensive.

Plague deaths were more numerous than in 1930; inoculation and rat destruction are the methods of choice while evacuation is also used in some districts.

Maternity and child welfare is run by the Lady Chelmsford League and Indian Red Cross Society. There are now 52 centres in towns and 72 in rural areas compared with 49 and 47 in 1930. The activities nevertheless were hampered by loss of funds due to financial depression.

The public analyst reports that the work of the Food Adulteration Act is hampered by the inadequate fines administered by magistrates in food adulteration cases, and by the shortage of staff under his control. School

appointed as officiating Assistant Director, Central Research Institute, Kasauli, with effect from 17th December, 1932, or the date on which he assumes charge of his duties.

Subject to His Majesty's approval, the undermentioned officers whose appointment on probation was notified in the London Gazettes dated 12th and 19th February, 1932, are confirmed in the following order on passing the necessary courses of instruction:—

Captains

R. A. Wesson; W. Happer; J. J. Quinlan.

Lieutenants

R. J. Jarvie; W. A. N. Marrow; F. A. B. Sheppard; M. Sendak; R. I. Reid; F. C. Jackson.

LEAVE

Lieutenant-Colonel R. Knowles, Professor of Protozoology, School of Tropical Medicine, Calcutta, is allowed leave for 2 months and 25 days, in extension of the leave granted to him in the previous notification.

Lieutenant-Colonel E. H. V. Hodge, Civil Surgeon, Howrah, is granted leave on average pay for 6 months, with effect from the 17th November, 1932. This cancels previous notification.

PROMOTIONS

Lieutenant to be Captain (provl.)

D. J. Young. Dated 30th September, 1932.

Lieutenant (on prob.) to be Captain (provl.) (on prob.)

B. L. Taneja. Dated 19th November, 1932.

The seniority of Lieutenant (on prob.) J. D. Grant is antedated to 20th April, 1931.

RESIGNATION

The Governor-General is pleased to accept the resignation by the Honourable Major-General J. W. D. Megaw, C.I.E., K.H.F., of his office of Member of the Council of State.

RETIREMENT

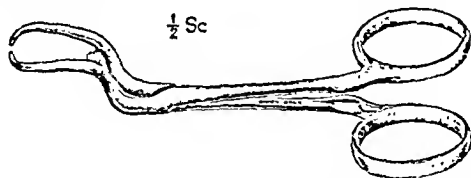
Lieutenant-Colonel R. H. Bott, C.I.E., retires 10th November, 1932.

Notes

SPECIAL TONGUE FORCEPS

By J. B. BLAIKLEY, F.R.C.S.

THE small tongue forceps illustrated have been made for me by Messrs. Down Bros., Ltd., for use in the resuscitation of new-born infants.



The chief advantage claimed for this instrument is that once the tongue is pulled forward the forceps holds it there by its own weight.

Corbould introduced self-retaining tongue forceps, but not of a suitably light pattern necessary when applied to an infant. The use of these forceps ensures a clear airway once all mucus is aspirated, while dispensing with an extra hand necessary to hold the forceps; this is particularly of value when carbon dioxide is being administered from a sparklet apparatus by means of a rubber face mask, which fits neatly over the proximal portion of the forceps.

In artificial respiration of an infant the operator is not embarrassed by a second person's hand over the chest holding the tongue forwards.

FOCAL INFECTIONS

UNDER the above title the British Hanovia Quartz Lamp Co., Slough, England, have issued a little booklet dealing with the use of actinotherapy in focal infections. These embrace such widespread and different conditions as diseases of the throat, nose and ear, adenitis

and tonsillitis, the use of ultra-violet rays to abort a cold, sinusitis, furunculosis, erysipelas, ringworm, the healing of wounds, etc.

The booklet can be obtained free by any Indian medical practitioner on application to the following agents:—

Messrs. Malgham Bros., 26, Custom House Road, Fort, Bombay.

Messrs. L. G. Vimar, Bijli House, 38, New Theatre Road, Calcutta.

Messrs. Adair, Dutt & Co., Keleeli Mansions, Mount Road, Madras.

SCHERING-KAHLBAUM, A.G., BERLIN

THE well-known continental firm of manufacturing chemists, Schering-Kahlbaum, have recently celebrated their 60th anniversary. In 1927, the firm of Kahlbaum was merged with that of the original concern, E. Schering, which was founded in 1861. They have recently issued an attractive booklet in which there is a short history of the gradual evolution of modern pharmacy from the times of the Chaldaic magicians, through periods of alchemism and sorcery, to the present-day period of carefully-standardised natural and synthetic medical preparations. The subject is an epic one and must appeal to all interested in human progress.

The manufacturing chemist of to-day is not content merely to place on the market a pure and standardised form of the pharmacopœial drugs, but employs an army of chemists and pharmacologists who are continually experimenting with new preparations. The Schering-Kahlbaum list of their original preparations is far too long to quote here and most readers will be familiar with them; amongst the most outstanding are urotropin, neotropin, veramon and atophan, names so familiar to the physician of to-day that he scarcely realises that they are proprietary drugs.

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Original Articles

NOTES ON MAKING EPIDEMIC FORECASTS

By SIR LEONARD ROGERS, K.C.S.I., M.D., F.R.C.P., F.R.S.
MAJOR-GENERAL, I.M.S. (ret'd.)

At the beginning of each of the last three years and again this year I have submitted forecasts of the probable incidence during the succeeding year of India's three most important epidemic diseases, cholera, smallpox and plague. Each forecast has proved to be very accurate. These forecasts were the outcome of a study of the relationship between certain climatic occurrences and the incidence of these diseases during the last sixty years, and were based on climatic data sent from India to me in London.

As I shall not much longer have ready access to the necessary data I propose to give in this paper the information required to enable the forecasts to be worked out in India itself by Public Health Commissioners or others who may possibly be sufficiently interested in the subject to test for themselves, at the cost of a few minutes a month, if my methods have any value or not. For this purpose I have given in a table the necessary climatic data, which can be filled in each month from the data published in the monthly weather reports of the Director-General of Observatories, Poona. In my own tables I enter the climatic data favouring increased prevalence of cholera and smallpox in bold type, and those indicating low prevalence in green ink; this allows the general tendency of the data to be seen at a glance. In the table the variations from the normal, of sufficient degree to be likely to influence subsequent increases or decreases of the prevalence of the three epidemic diseases dealt with, are shown in larger type to allow the explanations given below to be followed readily. If anyone in India is willing to test my methods I shall be glad to give him any further information in my power that he may require.

The climatic data used in forecasting and methods of obtaining them

In my first forecast, which appeared in the *Indian Medical Gazette* of March 1930, I summarised the climatic data on which the forecasts in my former papers are based, and I now illustrate them by the data (*vide* table) of two years in the Punjab, selected to show the climatic factors related to increased and decreased incidence, respectively, of cholera, smallpox and plague. The monthly variations from the average figures of a number of years are given for (1) the mean monthly temperature, (2) the mean 8-hours monthly relative humidity, (3) the mean vapour tension, or absolute humidity, at 8 hours, (4) the mean

monthly saturation deficiency calculated from (1) and (3), and (5) the monthly rainfall in inches. In my own tables the actual monthly data are also inserted, but are omitted from the table here for simplicity's sake. Below the data of each year are shown the monthly death rates per 100,000, the annual total deaths and the death rates per mille for cholera, smallpox and plague, respectively, for the *following year*. These are worked out from the numbers recorded in the annual provincial sanitary reports, and in preparing tables of them for several decades I found it saved much time if tables were first made of the rates per 100,000 from 0.1 to 10.0 with the aid of the millions of inhabitants of each area of each decennial census, which are given in the sanitary reports, as from these the ordinary monthly rates can be seen at a glance and those over 10.0 are quickly calculated.

Sources and methods of calculating the required climatic data

The necessary data can all be obtained directly or indirectly from the monthly weather reports published a few days after the end of each month by the Director-General of Observatories, Poona, to whom I wish once more to acknowledge my great indebtedness for supplying me with absolute humidity figures for several decades and many other data. In my studies of over half a century past I used the monthly temperature and rainfall records of a central station in each province, taken from the records still published in annual reports of the Sanitary Commissioner with the Government of India some two years after the periods to which they relate. In preparing forecasting tables the up-to-date monthly weather reports are essential, and either the figures of a central place in a province or area, or, better still, those of each province or area being dealt with, can be obtained from these reports as follows:—

(1) *The mean monthly temperatures* are obtained by adding together the mean 8-hours maximum and minimum temperatures and dividing by two. To obtain the actual figures for each province or smaller area, the mean of the highest and lowest readings of the particular data required, recorded for the various places in each area, are taken in making the estimation, but the variations from the normal maximum and minimum monthly temperatures are given both for provinces and for sub-divisions in the monthly reports, from which the monthly departures from the normal mean temperatures can be calculated and entered at once in the forecasting table under the appropriate month.

(2) *The monthly relative humidities* are also given in the same reports for a number of places in each province, the means of which will give the provincial and sub-divisional data, while the departures from the normals can be

taken directly from the first two tables of the report.

(3) *The mean vapour tension, or absolute humidities*, are not published in the monthly weather reports, but their departures from the normal are recorded in table 7 of the Indian weather review annual summary, but as these are not available until a year or so later they must be calculated for the forecasting tables from other data in the monthly weather reports; namely, the wet and dry bulb readings, the means of those of the different provinces and sub-divisions being taken when their absolute humidities are required. The wet-bulb 8-hours mean and the difference between that figure and the dry-bulb mean thus obtained will enable the absolute humidity of the nearest whole numbers to be found from nos. X and XI of 'Tables for the reduction of meteorological observations in India' published by the department in 1910, that table calculated for the nearest barometrical readings to those of the province being dealt with being selected, and the slight differences for the fractions of a degree in the wet bulb and difference from the dry bulb are easily estimated from the data in the tables mentioned.

(4) *The saturation deficiencies* can then be readily worked out by taking the figure of the saturation point of the mean temperature of the month from table IX, of the same publication, of vapour pressures and subtracting the absolute humidity figure from it. The saturation-deficiency figure thus obtained is a measure of the drying power of the air, a high figure meaning a great drying power, and *vice versa*. I found it convenient to amplify table IX with the data of each 0.1 of a degree between those given in the table for each 0.2 of a degree for the temperatures requiring to be used. Doubtless the Indian meteorological department will be glad to supply public health officers each month with any such data for their province.

(5) *The monthly rainfalls* and their departures from the normals can also be taken straight from the monthly weather reports.

The climatic factors influencing the subsequent prevalence of cholera, smallpox and plague respectively

In order to illustrate the climatic factors favourable to and adverse to increased cholera, smallpox and plague, respectively, I have selected the data of the Punjab in 1917 and 1918 on account of the unusually wide variations from the normal they showed, followed by the epidemic prevalence of the diseases dealt with, but it must be remembered that the Punjab shows the greatest variations of all the provinces of India in both climatic conditions and the prevalence of epidemics, and lesser variations of the climatic data from the normal may be of significance in forecasting.

Increased cholera prevalence in 1919 following low 1918 monsoon rains

In my table the major variations from the normal in the meteorological data which influenced subsequent disease incidence are shown in larger figures to enable the description to be followed more easily. The significance of *plus* and *minus* data on each disease is also indicated in the table. In my comprehensive study of some sixty years, monthly cholera and climatic data recorded in the *Indian Journal of Medical Research Memoirs*, No. 9 of March 1928, I showed that no less than 40 of the 41 cholera epidemics in various parts of India during a period of forty-five years, the outbreaks followed deficient rainfall in the areas affected during the previous year's monsoon, and often also in the following winter months, while the single exception was due to the Allahabad Kumbh Fair of 1894. The table illustrates such an epidemic in the Punjab in 1919 following a deficit of 8.23 inches of rain, or 42 per cent of the total, in 1918, and a deficit of 7.79 inches, or 52 per cent, in the monsoon quarter of July to September; the monthly figures for Lahore showed only 5.64 inches in those three monsoon months against a normal of 13.43. As usual cholera only broke out in the Punjab in April of the following year, when the monthly absolute humidity there first rises above 0.400 (below which point I showed in my memoir that cholera never becomes widely prevalent in any province of India) and the disease became widespread at the usual Punjab cholera season of June to September, with 8,561 deaths, or 0.44 per mille, for the year, against a five-yearly average from 1916 to 1920, including an epidemic year, of 0.12 per mille.

Low cholera following heavy monsoon rains in the previous year

The table also furnishes an example of the very high rainfall of 1917 of 36.79 inches, an excess of no less than 16.93 inches, or 85 per cent, being followed by the very low figure of 257 cholera deaths in 1918, or 0.01 per mille, one of the lowest Punjab rates on record.

Epidemic smallpox in 1919 following low monsoon and autumn absolute humidities in 1918

In my study of nearly half a century's monthly records of smallpox in the different provinces of India in relation to the climatic data (*Medical Research Council Special Report Series*, No. 106, 1926) I showed that in the seven provinces that received the full effects of the south-west monsoon the disease reaches its yearly minimum during the high absolute humidity of that season, but the incidence remains high in most of Madras which gets little of the south-west monsoon rain. Further, the worst outbreaks of smallpox occur in north-west and central India in the year following a failure of the monsoon in those areas, which are most

jab 1917-1919

Oct.	Nov.	Dec.			
			Total annual	Departure from annual mean	
- 2.9	- 4.3	- 0.7	..	- 2.2	- mean temperature = + plague.
+ 18	+ 10	+ 11	..	+ 7	+ relative humidity = - smallpox.
+ 0.120	- 0.004	+ 0.036	..	+ 0.037	+ absolute humidity = - smallpox.
- 0.210	- 0.067	- 0.031	- saturation deficiency = + plague.
+ 2.68			36.79	+ 16.93	+ rainfall = - cholera.
			Total cases	Rate per mille	
..	257	0.01	- cholera.
1.0	1.7	5.0	3,032	0.16	- smallpox.
0.1	0.2	0.8	95,615	4.94	+ plague.
			Total annual	Departure from annual mean	
+ 0.4	- 0.4	- 0.9	..	+ 0.3	+ mean temperature = - plague.
- 6	- 7	0	..	- 3	- relative humidity = + smallpox.
- 0.067	- 0.038	- 0.004	..	- 0.023	- absolute humidity = + smallpox.
+ 0.019	+ 0.039	- 0.024	+ saturation deficiency = - plague.
- 0.38			11.57	- 8.23	- rainfall = + cholera.
			Total cases	Rate per mille	
0.5	8,561	0.44	+ cholera.
1.8	3.6	7.1	15,365	0.79	+ smallpox.
1.0	0.9	0.6	11,068	0.57	- plague.

TABLE I
epidemiological da

July	August	
- 0.9	- 2.6	-
+ 3	+ 9	-
+ 0.030	+ 0.063	-
- 0.042	- 0.203	-
+ 14.42		
0.4	0.3	
0.9	1.2	
2.1	0.1	
+ 3.8	+ 3.0	-
- 14	- 9	-
- 0.103	- 0.074	-
+ 0.288	+ 0.198	-
- 7.79		
18.8	7.3	
9.3	4.1	
0.3	0.1	

(Continued at foot of next column)

tion deficiency in May 1910 as usual.

closely correlated with low average monsoon and autumn absolute humidity due to short rains, as the annual monsoon decline is less, and the regular smallpox rise in November and December starts from a higher level with resulting high rates throughout the ensuing winter and hot weather seasons, until the full establishment of the next monsoon rains brings it down again. This sequence of events is well illustrated by the absolute humidity data of 1918 and the smallpox rates of 1919 in the lower half of the table, for the monsoon and absolute humidity rates from July to November were exceptionally low, and the smallpox incidence rose rapidly to well above the average for that month in December 1918 and continued above the average through 1919, with the maximum as usual in the hot season; 15,365 deaths, or 0.79 per mille, were recorded in 1919, against an average of 0.12 per mille in the previous five non-epidemic years.

Low smallpox following previous high monsoon absolute humidity

On the contrary, the very high absolute humidity from May to October 1917, accompanying the excessive rains of that year, was followed by low smallpox incidence in the first nine months of 1918, during which year 3,032 deaths were recorded, no less than 1,544 of which were in the last quarter of the year following low monsoon absolute humidity of the 1918 monsoon, against only 285 in that quarter of 1917.

High plague incidence in 1918 following low temperatures in the hot season and low saturation deficiencies in 1917

In my study of 23 years plague records in India in relation to climate (*Proceedings of the Royal Society, Series B, Vol. 103, p. 42*) I showed that low monthly mean temperatures in the hot weather and monsoon seasons, and low saturation deficiencies at all times of the year, are likely to be followed by high plague incidence. On the contrary, high hot weather temperatures and high saturation deficiencies are followed by decreased plague; doubtless owing to their unfavourable influence on the life of plague-infected rat fleas which convey the disease to man. As the latter conditions occur especially in years of low rainfall and low monsoon absolute humidity, it is clear that decreased plague is probable in years favourable to increased cholera and smallpox, as is illustrated in the table. Thus the low rainfall and absolute humidities in 1918, followed by high cholera and smallpox, were accompanied as usual by high temperatures and saturation deficiencies with consequent comparatively low plague incidence in 1919, 11,068 deaths, or 0.57 per mille, against an average for the previous five years of 4.07 per mille which included the epidemic year 1915. On the other hand, in

(Continued at foot of next column)

MALIGNANT DISEASE IN THE PUNJAB

By VISHWA NATH, M.A., M.D., F.R.C.P.I.,
D.P.H., D.T.M. & H.

RAI BAHADUR JIWAN LALL, M.D., B.S.

and

JAGAT SINGH, M.B., B.S.

*Department of Pathology, King Edward Medical College,
Lahore*

No idea of the mortality from malignant disease can be formed from the vital statistics published for India as a whole, or from the statistics of her constituent provinces. It is still more difficult to form an idea of the morbidity due to malignant disease. So far as the cancer portion of malignant disease is concerned, enthusiasts publish from time to time statistics to suit their own theories, but wherefrom and how they get their figures seldom receives consideration. For example Marwood (1926) trying to prove the association between the salt consumption of a country and its cancer mortality states the cancer death-rate for India and China to be 11.7 and 8.1 per hundred thousand and for the United Kingdom and the United States of America 121.5 and 100 per hundred thousand, respectively. His statistics for the western countries may be correct, but those regarding India and China can only be conjectural. Others base their impressions of lower incidence and mortality of cancer in India on lack of "civilization", (Vedder, 1927), peculiarities or insufficiency of diet, etc., but all such theses are mere assertions based on little or no investigation.

Vital statistics in India are not based on death certificates issued by qualified medical practitioners. Nine-tenths of the population is settled in villages; a great majority of these

(Continued from previous column)

1917 the high rainfall and absolute humidity were naturally accompanied by low mean temperatures from April to November, and low saturation deficiencies from May to October, with the result that the plague incidence did not decline as much as usual in the late hot weather and monsoon months of 1917, it rose above the average during the last quarter of that year, and reached epidemic prevalence during the usual yearly maximum season in the first five months of 1918, with 95,615 deaths in the year, or 4.94 per mille; this figure would be still higher if the figures for the twelve months from October 1917 to September 1918 are taken. The 1918 plague deaths were just ten times the average of the two preceding and four subsequent non-epidemic years, and the highest rates occurred in relation to low mean temperatures and saturation deficiencies in March and April of that year, and the rate declined with unusual rapidity in June, after exceptional high mean temperature and saturation deficiency in May 1918 as usual.

cannot and do not support a doctor of any description. The village watchman (chowkidar), poor and illiterate, is the diagnostician who reports to the nearest police station once or twice a month the deaths occurring in his area and the causes as he knows them. It is this information which is the foundation of Indian vital statistics. Even in urban areas well served by qualified medical practitioners, it has not yet proved practicable to introduce proper certification of deaths.

Crude as they are, these statistics cannot, however, be regarded as valueless for all purposes. Epidemic diseases still form the most important factor in Indian mortality and even a village watchman may be trusted to report, more or less correctly, deaths from diseases like plague and cholera when they appear in epidemic form and although headings like "respiratory diseases" and "fevers" as causes of death may fall short of western standards of vital statistics, their analysis by capable epidemiologists has yielded data which not only form valuable contributions to epidemiology, but have even encouraged philosophical speculation in search of a unity of mechanism behind different epidemic diseases (Gill, 1928).

In the assessment of cancer mortality, however, these statistics are not only no help, but a definite hindrance. With epidemic and non-epidemic infectious diseases so common in the country, not many cancer patients—with their vitality diminished—can escape death from prevailing infections, which are then naturally recorded as the cause of death. The anaemia, emaciation and cachexia, obvious enough for a village chowkidar to see, are also and more commonly features of chronic infectious and parasitic diseases in India, and these mask cancer mortality not only in rural but also in urban areas. Few of the practitioners of the indigenous systems of medicine, whose contact with the Indian public is undoubtedly more intimate, will recognise cancer. The staff of charitable hospitals apart, the clientèle of the medical practitioner, trained in western scientific medicine, is drawn mainly from the comparatively literate section of the population. Some knowledge regarding cancer, therefore, does exist in this section of the lay public. The great mass of the unlettered population, however, is not aware of cancer as a disease in the way that it is of plague, cholera, dysentery, malaria, etc.

The literature published from India on malignant disease is meagre. Neve (1902) published a paper on a "Decade of tumour surgery in Kashmere Mission Hospital", in which he brought out the importance of long-continued irritation caused by kangri burns in the aetiology of kangri cancer. Sutherland (1904) published a paper on "Statistics of malignant disease admitted to the Mayo Hospital, Lahore, from 1892-1903", in which he showed that of 43,412 cases admitted to the

hospital during those twelve years, 792 were cases of malignant disease, which he classified as follows:—"Carcinoma 400, sarcoma 334, abdominal growths 35, and malignant growths 23".

Amongst the cancer cases 58 were epitheliomas and 36 rodent ulcers. He attributed scalp cancers amongst Mohammedans to the irritation from blunt razors used in shaving their heads. Amongst recent contributions dealing with cancer in India are two papers concerned with the examination of material from Pathology museums in Madras (Basu and Vasudevan, 1929) and Bombay (Gharpure, 1927) medical colleges, and Sir Leonard Rogers' Lettsonian Lectures in 1925, giving an analysis of 1,190 cases examined in Calcutta, 579 of which were malignant and 421 non-malignant. Certain annual reports also occasionally bring out facts regarding prevalence of malignant disease. For instance the "Annual report and statistics, Government General Hospital, Madras, for 1927" showed that 13,158 patients were admitted to the hospital that year. Six thousand three hundred and forty-six out of this number were admitted to the surgical ward and of these 258 suffered from malignant disease—177 from cancer and 24 from sarcomas.

Megaw and Gupta (1927) issued a questionnaire to all civil surgeons in medical charge of districts in India. This was an attempt, not to obtain statistical information which would have failed, but just to know whether particular diseases were "common", "rare" or "unknown" in different districts. Information obtained regarding distribution of cancer through this questionnaire was valuable, although replies of some of the medical officers who returned certain types of cancer as "unknown" in their districts must either have been casual or their opportunities of seeing patients limited. Information was called for in respect of cancer of the breast, uterus, stomach, mouth and skin. From the Punjab 21 medical officers answered the questionnaire and of these as many as eight affirmed that cancer of the skin was "unknown" in their districts—a statement very difficult to believe. On the other hand the statement that cancer of the stomach was "unknown" in as many as 15 districts, "rare" in six and "common" in none is not incredible, knowing as we do how rarely do surgeons and pathologists meet with this lesion in the Punjab.

In western countries the view is expressed that so far as cancer mortality is concerned, it will not attain a desired standard of accuracy until a very much larger proportion of vital statistics depends on autopsy findings than is the case at present (Gideon Wells, 1923). Error in diagnosis in internal tumours is said to be as high as 37.1 per cent. in the United States of America and 37.3 per cent. in England.

In 1902 Reichelmann showed in Berlin by an analysis of 7,790 autopsy records that of

cases diagnosed "cancer" at autopsy 22 per cent. had not been recognised as suffering from that disease during life (Vedder, 1927).

Table I gives an idea of comparative incidence of cancer found on post-mortem examination in certain non-European countries :—

TABLE I

Number		Punjab	Porto Rico	Haiti (Choisser, 1930)	Java (Sitsen, 1928)	Philippines, Manila (Vedder, 1927)
1	Total number of autopsies ..	329	120	700	3,025	8,960
2	Number of autopsies in which malignant disease found.	14	7	27	75	233
3	No. 2 expressed as a percentage of No. 1.	4.25	5.83	3.43	2.5	2.6

In India not only are the basic records on which vital statistics based poor, but any better view which could be obtained of the causation of death, through post-mortem examinations, is also unattainable. So great is the prejudice on the part of relations to submitting the dead to a post-mortem examination, that post-mortem pathological investigation is possible only on stray unclaimed bodies.

The institution from which this paper is issued is part of the biggest teaching hospital in the Punjab and yet between 1921 and 1931 (both years included) only 329 post-mortems were carried out for pathological investigation. Malignant disease was diagnosed in 14 cases in this series. Of these 14 ten were carcinomas, one lymphosarcoma, two other sarcomas and one pulmonary growth secondary to a teratoma testis.

The distribution according to organs was as follows :—

Carcinoma	Sarcoma	Teratoma
Liver 1	Rib 1	Testis with
Stomach 2	Generalised 1	metastases in
Esophagus 1	Lymphosarcoma 1	lung 1
Pancreas 1		
Lung (Primary bronchogenic) 1		
Bladder 3		
Kidney 1		

These statistics, although too meagre to warrant any generalizations, nevertheless go to show that malignant disease is not an unimportant factor in mortality amongst people of non-European descent.

Some idea of the incidence of cancer amongst these people may also be obtained from statistics of biopsy examinations. Analysis of some Indian material by Sir Leonard Rogers has already been referred to. The following statistics of biopsy examinations carried out in the pathological department of the King Edward Medical College, Lahore, are given to afford some idea of the extent to which malignant disease contributed to the material examined.

Total number of specimens examined histologically from 1922 to 1931	3,850
Non-neoplastic	2,309
Neoplastic	1,541
Innocent new growths ..	649
Malignant new growths ..	892
Carcinomata	634
Sarcomata	211
Other malignant neoplasms ..	47

A statement comparing the above statistics with those available from some other non-European countries is given below (table II) :—

TABLE II

Number		Punjab	ANNAM HOSPITALS			Java (Sitsen, 1928)	Mexico (Maxwell, 1928)
			Saigon (Bablet, 1926)	Cholon (Bablet, 1926)	Tonking (Bablet, 1932)		
1	Total number of new growths examined.	1,541	357	650	..	1,240	..
2	Number of malignant new growths examined.	892	128	178	784	629	1,133
3	Malignant growths expressed as a percentage of total number of new growths.	57.88	35.86	27.4	..	50.7	..
4	Proportion of carcinoma to sarcoma.	3 : 1	3.5 : 1	4 : 1	6.58 : 1	2.15 : 1	3.3 : 1

Table III gives the distribution of cancer and sarcoma according to sex, age and community. Many specimens come for examination without any particulars being furnished as to age, sex, community or clinical history. Of 845 cases, diagnosed cancer or sarcoma, information as to sex was available in 692 and as to sex, age and community in 536.

This table (III) shows that the incidence of cancer in the two sexes is about equal. The preponderance of breast and uterine cancers in the female is balanced by heavier incidence of skin, lip and tongue cancer in the male. Of 29 specimens of rodent ulcer examined, information as to patients' sex was wanting in three. Of the remaining 26, 23 specimens came from male cases and only 3 from females. The age group with the highest incidence of cancer is

and outpatients' departments from 1923 to 1931. Out of this number histological confirmation of the clinical diagnosis was obtained in 523 cases. The opportunities for utilising the services of the pathology department of the college are exceptional so far as the Mayo Hospital is concerned, although the mofussil hospitals also use it in degree varying with the enthusiasm of the medical officers in charge. The proportion, therefore, of histologically-verified cases of malignancy to the total number of cases clinically diagnosed, i.e., 1:5, may be of interest when studying the figures of malignant disease as furnished by Government hospitals from all over the province. Table (V) compiled from the reports of the Inspector-General of Civil Hospitals, Punjab, from 1923 to 1931 gives the number of cases of malignant disease

TABLE IV

	Punjab	Manila (Vedder, 1927)	China	Mexico (Maxwell, 1928)	Porto Rico	Annam (Bablet, 1926)	Egypt (Dolbey and Moore, 1924)
Breast (per cent.) ..	14.8	11.15	18	18.19	10	8.3	11
Uterus and cervix (per cent.)	8.85	6.86	12	12.36	12.24	11	3.66
Penis (per cent.) ..	4.14	5.15	..	14.04	13	10	..

from 41 to 50 for both sexes. The highest incidence, therefore, occurs about a decade earlier than in Europe and North America. Over 90 per cent. of cases fall within the age group 21 to 60.

The above is not the case with sarcomas, in which the age period with highest incidence appears to be 21 to 30. The proportion between male and female incidence was about 2 to 1.

The comparative table (IV) may also prove of interest. The incidence in the organs considered is a percentage of the total number of specimens of malignant disease examined.

As regards incidence in different organs the following facts may be of interest in the Punjab statistics:—

The heaviest incidence of malignancy is on the breast 14.8 per cent. Skin cancers including rodent ulcer and cancer of the tongue constitute about 13 per cent. of the total. Female reproductive organs come next. Malignant growths of the liver and digestive tract together account for 4.8 per cent. The penis comes next with 4.14 per cent. Of 93 senile prostates examined 16 were cancerous. Nine tumours of the thyroid were found to be malignant. Of benign tumours uterine fibroid accounted for 8 per cent.

In the Mayo Hospital, Lahore, which is attached for teaching purposes to the King Edward Medical College, Lahore, 2,775 cases of malignant disease were treated in the wards

treated in the Government hospitals of each district of the province. It also gives the number of deaths from malignant disease which took place in the Government hospitals of each district. This mortality must not be taken, however, as representing either the total fatalities from this cause or the percentage of inoperable cases which come for relief to these hospitals. If it represents anything at all, it represents mortality under operation and the very small margin of accommodation available in State hospitals for incurable and moribund cases.

Another table giving similar information from the Mayo Hospital, Lahore, is also given. It tabulates separately cases of malignant disease treated in the outdoor and indoor departments of the hospital. As a background to these statistics of malignant disease the total number of indoor and outdoor patients treated each year is also given.

In the table for the whole province (table V), it will be noticed that the highest figures for malignant disease obtain in the districts of Ludhiana, Ferozepur, Lahore and Amritsar. Hissar also shows a higher level than many other districts. The excess in the districts mentioned cannot be taken to mean a higher incidence of malignant disease in those localities, but only the presence of better hospital and laboratory aid, so that patients are attracted to these centres from other districts as well.

The material contained in this paper can afford no information as to the exact position

TABLE III

Type of malignant tumour	Sex	Community	AGE GROUPS								Age not known	Total
			1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
Carcinomata	Male	Hindu	2	1	14	20	31	21	4	1	1	108
		Muslim	2	0	14	17	25	12	6	3	1	87
		Sikh	0	0	8	11	10	4	1	1	0	40
		European	0	0	0	1	4	1	1	0	0	11
		Others	1	0	0	4	3	4	0	0	0	27
		TOTAL FOR EACH AGE GROUP.	5	1	36	53	73	42	12	5	2	273
	Female	Hindu	0	7	15	40	31	9	1	0	1	105
		Muslim	1	1	9	8	25	5	0	0	0	59
		Sikh	0	0	1	4	2	4	0	1	0	18
		European	0	0	1	4	6	4	2	0	0	28
		Others	1	1	0	9	7	0	0	0	0	60
		TOTAL FOR EACH AGE GROUP.	2	9	26	65	71	22	3	1	1	270
	Male	Hindu	3	7	8	4	8	1	1	0	0	35
		Muslim	4	3	10	9	6	8	0	0	0	47
		Sikh	0	3	4	4	1	2	0	0	0	14
		European	0	0	0	0	0	0	0	0	0	0
		Others	1	1	0	0	0	0	0	0	0	5
		TOTAL FOR EACH AGE GROUP.	8	14	22	17	15	11	1	0	0	101
	Female	Hindu	0	3	9	6	2	0	0	0	0	24
		Muslim	3	2	2	1	3	1	0	0	0	15
		Sikh	0	0	0	0	0	0	0	0	0	1
		European	0	0	0	2	0	0	0	0	0	3
		Others	1	0	3	1	0	0	0	0	0	5
		TOTAL FOR EACH AGE GROUP.	4	5	14	10	5	1	0	0	0	48

of malignant disease in the vital statistics of this province. It can, however, testify to the definite presence of malignant disease in the province and its not insignificant rôle as a cause of mortality and morbidity. Although

TABLE V* (a)

Number of cases of new growths (malignant) treated in the Punjab from 1923 to 1931

Year	Total treated	Total deaths
1923	799	62
1924	1,951	51
1925	2,157	71
1926	2,235	72
1927	2,813	64
1928	2,953	87
1929	2,617	76
1930	2,691	63
1931	2,891	61

* Table V sent for publication was a detailed table, showing the two sets of figures year by year in each place; the necessity to economize space has compelled us to summarize these figures and to give them in two separate tables V(a) and V(b).

TABLE V (b)

Number of cases of new growths (malignant) treated in the various districts of the Punjab from 1923 to 1931

Districts	Total treated	Total deaths
Hissar ..	1,093	17
Rohtak ..	335	6
Gurgaon ..	714	22
Karnal ..	541	13
Ambala ..	766	26
Simla ..	342	27
Kangra ..	307	13
Hoshiarpur ..	498	8
Jullundur ..	696	14
Ludhiana ..	1,081	73
Ferozepur ..	1,002	42
Lahore ..	3,902	166
Amritsar ..	2,156	62
Gurdaspur ..	332	9
Sialkot ..	541	7
Gujranwala ..	908	3
Sheikhupura ..	256	3
Gujrat ..	528	10
Shahpur ..	621	10
Jhelum ..	402	5
Rawalpindi ..	359	11
Attock ..	414	2
Mianwali ..	229	3
Montgomery ..	426	6
Lyallpur ..	431	10
Jhang ..	509	5
Multan ..	737	20
Muzaffargarh ..	251	7
Dera Ghazi Khan ..	392	4
Railways ..	70	1

the autopsy and biopsy figures handled are small, the inference is not unjustifiable that the incidence of carcinoma in the two sexes is about equal, that the age period for highest

TABLE VI

Year	TOTAL NUMBER OF PATIENTS TREATED		TOTAL NUMBER OF CASES OF MALIGNANT DISEASE TREATED	
	Out-door	In-door	Out-door	In-door
1923	34,872	5,604	119	156
1924	33,524	5,743	92	152
1925	36,955	6,720	139	153
1926	37,777	7,158	122	127
1927	41,459	7,506	193	194
1928	45,380	7,622	211	142
1929	46,625	7,568	164	93
1930	53,435	7,912	188	123
1931	57,387	8,044	248	159

incidence of cancer is from 40 to 50, and not from 50 to 60, as is the case in Japan, most European countries and the United States of America, and that cancer of the breast and reproductive organs is commonest among females and of surface epithelium in the male. The figure for cancer of the penis is not as high as in some other countries, and cancer of the gastro-intestinal tract and liver is not so common as in the Far East, the Dutch Indies and probably in Southern India. The proportion of carcinomata to sarcomata is, as in some other countries, about 3:1. The maximum incidence of sarcomata is, as in the Chinese and Europeans, at a younger period (20 to 30). The incidence is not, more or less equally, distributed over all age periods, as is said to be the case among the Javanese.

Until such time as economic and educational progress makes it possible for proper vital statistics to be collected in this country, reports of autopsy and biopsy examinations ought to be obtained by some central agency from all pathological laboratories in India and statistics affording an insight into the problem of malignant disease obtained. In suspected cases of malignancy it should be made possible for any registered medical practitioner in attendance to obtain free of charge from any Government pathological laboratory a report on material submitted for histological examination.

REFERENCES

- Bablet, J. (1926). Sur la Fréquence et les Modalités du Cancer chez Annamites de Cochinchine. *Ann. Inst. Pasteur*, Vol. XL, p. 922.
- Bablet, J. (1932). Sur la Fréquence et les Modalités du Cancer chez les Annamites du Tonkin. *Ann. Inst. Pasteur*, Vol. XLVIII, p. 594.
- Basu, P. N., and Vasudevan, A. (1929). Primary Carcinoma of Liver in South India. *Journ. Path. and Bact.*, Vol. XXXII, p. 342.
- Choisser, R. M. (1929). Pathology in the Tropics. A Study based on the Review of 700 consecutive Autopsies in Haiti. *United States Nav. Med. Bull.*, Vol. XXVII, p. 551. (Abstracted in the *Bull. Hyg.*, 1930, Vol. V, p. 300.)
- Cox, J. W. (1931). The Cancer Control Programme. *New Orleans Med. Surg. Journ.*, Vol. LXXXIV, p. 455. (Abstracted in the *Bull. Hyg.*, Vol. VII, p. 229.)

Dolbey, R. V., and Mooro, A. W. (1924). The Incidence of Cancer in Egypt. *Lancet*, Vol. I, p. 587.

Gharpure, P. V. (1927). Incidence of Primary Carcinoma in India as inferred from Post-mortem Records of Fifty Years from 1877-1926. *Indian Med. Gaz.*, Vol. LXII, p. 315.

Gideon Wells, H. (1923). Relation of Clinical to Necropsy Diagnosis in Cancer and Value of existing Cancer Statistics. *Journ. Amer. Med. Assoc.*, Vol. LXXX, p. 737.

Gill, C. A. (1928). *The Genesis of Epidemics*. London: Baillière, Tindall & Cox.

Marwood (1926). Salt and Cancer. *Medical Officer*, Vol. V, p. 35.

Maxwell, J. L. (1928). Cancer Among the Chinese. *China Med. Journ.*, Vol. XLII, p. 69.

Megaw, J. W. D., and Gupta, J. C. (1927). The Geographical Distribution of Some of the Diseases in India. *Indian Med. Gaz.*, Vol. LXII, p. 299.

Neve, E. F. (1902). Decade of Tumour Surgery in Kashmere Mission Hospital. *Indian Med. Gaz.*, Vol. XXXVII, p. 164.

Sitsen, A. E. (1928). Fourteen Years New Growth Investigation in Sourabaya (Java). *Nederl. Tijdschr. Geneesk.*, Vol. LXXII, First Half, p. 285. (Abstracted in the *Bull. Hyg.*, Vol. III, p. 761.)

Sutherland, D. W. (1904). Statistics of Malignant Disease admitted to the Mayo Hospital, Lahore, India, from 1892 to 1903 inclusive. *Arch. Middlesex Hospital*, p. 81. Third Report from the Cancer Research Laboratories.

Vedder, E. B. (1927). The Incidence of Cancer in Filipinos. *Journ. Amer. Med. Assoc.*, Vol. LXXXVIII, p. 1627.

A NOTE ON THE USE OF MARMITE IN TROPICAL MACROCYTIC ANÆMIA, INCLUDING PERNICIOUS ANÆMIA OF PREGNANCY

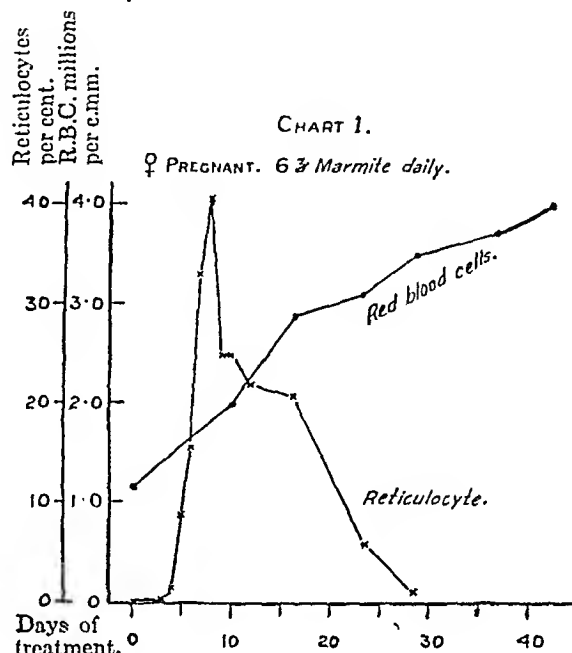
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In an earlier paper the use of *Marmite*, a yeast extract, in the treatment of tropical macrocytic anæmia was reported (Wills, 1931). Since this publication other workers have recorded varying results with this line of treatment. Vaughan and Hunter (1932), Goodall (1932), and others have reported success both in macrocytic anæmia in cases of idiopathic steatorrhœa, and in certain cases of true pernicious anæmia. Mudaliar (1932) reports unfavourably from Madras, Green-Armytage (1932) favourably from Calcutta. Unpublished figures from other parts of India are favourable.

In a paper to be published shortly a full account of the treatment of this anæmia will be given, but as further trials have confirmed my previous findings as to the curative action of this preparation, the following notes as to its use and limitations may be helpful to other workers, wishing to make a trial of this remedy.

1. It is essential that the diagnosis of pernicious anæmia of pregnancy or tropical macrocytic anæmia should be made on an accurate examination of the blood picture. Experience in Bombay suggests that both marmite and liver extract are used very frequently in microcytic secondary anæmias, mistakenly diagnosed as pernicious anæmia on the clinical picture.



Negative results are regarded as evidence of the uselessness of these remedies, a revision of the diagnosis being but rarely considered.

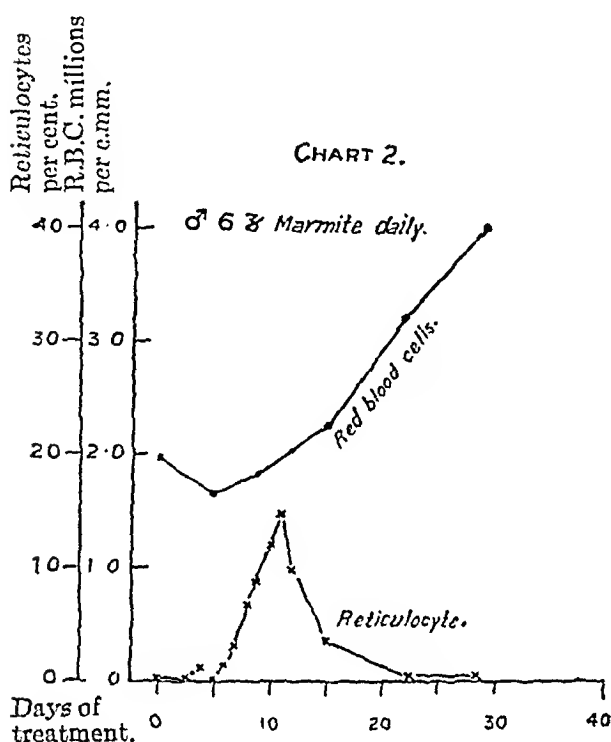
2. Sepsis as a complication must be excluded, and this applies particularly to post-delivery cases, as severe sepsis is well known to inhibit the hæmopoietic effect of both liver extract and marmite.

3. If the response to treatment is to be judged by the reticulocyte rise, reticulocyte counts must be made daily from the third to the tenth day. One worker who reported unfavourably on the curative action of marmite on this basis, in a personal communication said that the reticulocyte count had been made only on or about the tenth or fourteenth day.

4. Marmite to be active must be used in adequate doses and it is essential to see that the dose prescribed is both given and taken. Again from experience in Bombay hospitals, the need for personal supervision in this respect is stressed. In severe cases I am now giving two-drachm doses three times a day. Goodall's patients took half an ounce, three times a day. Vomiting rarely occurs if the medical adviser personally sees that the dose is properly given. Diluted with three or more ounces of iced water, with ice or sour lime to suck immediately after, it rarely causes nausea, especially if the patient is reassured. Given as a soup, with

the addition of some vegetable or meat stock, well flavoured to taste, many patients like it and find it appetizing.

5. In desperately ill cases, when digestion and absorption are very greatly reduced or absent and time is of the greatest importance, the best line of treatment is intramuscular or intravenous injections of liver extract combined when possible with a small transfusion. After the first few days, if there is any response, the injections may be replaced by liver or marmite by mouth. But in the majority of cases, even



those with counts as low as one million, the response to marmite in adequate doses is so rapid that the more expensive treatment is rarely necessary.

6. A few cases may not respond to treatment with marmite, when it may be assumed that the intrinsic factor of Castle (1929 and 1930) is missing. Such cases are extremely rare in Bombay; hidden sepsis is a far more frequent cause of failure.

The response to treatment in two typical cases is shown in the accompanying charts.

REFERENCES

- Castle, W. B. (1929). *Amer. Journ. Med. Sci.*, Vol. CLXXVIII, p. 748.
 Castle, W. B., and Townsend, W. C. (1929). *Ibid.*, p. 764.
 Castle, W. B., Townsend, W. C., and Heath, C. W. (1930). *Amer. Journ. Med. Sci.*, Vol. CLXXX, p. 305.
 Goodall, A. (1932). *Lancet*, Vol. II, p. 781.
 Green-Armytage, V. B. (1932). *Indian Med. Gaz.*, Vol. LXVII, p. 144.
 Mudaliar, A. L., and Rao, K. N. (1932). *Indian Journ. Med. Res.*, Vol. XX, p. 435.
 Vaughan, J. M., and Hunter, D. (1932). *Lancet*, Vol. I, p. 829.
 Wills, L. (1931). *Brit. Med. Journ.*, Vol. I, p. 1059.

INTENSIVE IRON TREATMENT OF ANÆMIA IN A TEA-GARDEN LABOUR FORCE*

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PRACTICALLY all anæmic patients are treated as in-patients. On the day of admission oil of chenopodium is given, which is repeated once weekly so long as the patient is in hospital. The iron treatment (*ferri et ammonii citras*) is started from the second day and continued until the hæmoglobin value of the patient's blood is 60 per cent. or higher.

We gave one drachm of *sodii sulphas* along with each dose of iron in a mixture to counteract constipation, but sometimes bigger doses of *sodii sulphas* are required. Purgatives can also be given separately, when necessary. In fact, a saline aperient is an essential accompaniment of this treatment. Other conditions were treated symptomatically as they arose.

Altogether 80 cases were treated. In order to study the effect of various doses they were divided into three groups. The first group consisted of 9 patients getting at the start a daily dose of 60 grains of *ferri et ammonii citras*, which was gradually increased to 90 grains daily. The second group consisted of 18 patients getting at the start a daily dose of 60 grains, which was gradually increased to 120 grains daily. The third group consisted of 53 patients getting at the start a dose of 90 grains daily, which was gradually increased to 120 grains daily. The hæmoglobin estimations were made by Tallqvist's scale. The details are shown in table I.

TABLE I

	Group 1	Group 2	Group 3	Average of 3 groups
Number of cases treated.	9	18	53	..
Average time on the anæmic list in months.	15.7	13.6	5.8	11.7
Average daily dose in grains.	70	94.2	97.3	87.2
Average hæmoglobin percentage on admission.	30	33.9	45.1	36.3
Average hæmoglobin percentage on discharge.	60	60.8	63.3	61.3
Average length of treatment in days.	28.4	18.8	10.8	19.3

The following facts emerge from the above table :—

- The chronicity of the cases.
- The low level of hæmoglobin percentage on admission.

* Rearranged by editor.

(c) The efficacy of iron—the bigger the dose, the better and quicker the result.

Table II has been prepared from group 3 only; of this group, 29 patients had hæmoglobin of 45 per cent. and less on admission, the average being 40.1 per cent.; the remaining 24 had hæmoglobin above 45 per cent. on

TABLE II

(Showing the difference in the effect of iron according to the degree of anæmia on admission.)

	HÆMOGLOBIN	
	45 per cent. or less	Over 45 per cent.
Number of cases treated ..	29	24
Average daily dose in grains ..	102.4	91.2
Average hæmoglobin percentage on admission.	40.1	51
Average hæmoglobin percentage on discharge.	62.4	64.4
Average length of treatment in days.	13.4	7.7

admission, the average being 51 per cent. All these 53 patients had uniform treatment, as shown above, that is the daily dose was started at 90 grains and increased to 120 grains. It is obvious from this table that the higher the percentage of hæmoglobin on admission, the quicker the result and the less the dosage required.

Influence of diet.—Owing to the present economic crisis, no special dietary could be arranged. The patients were given a little chicken soup thrice weekly in addition to the usual *dal* and vegetable curry; this was supplemented, when possible, by a little milk. Considering the modesty of the diet supplied, I have no reason to believe that the diet accentuated the effect of the iron.

Influence of sex.—This series consisted of 55 women and 25 men, that is the women formed 69 per cent. of the total cases; there was no difference in progress between the two sexes. Among females themselves, there was no difference in response between the unmarried, married, nulliparæ, primiparæ and multiparæ.

Influence of age.—The average age of women was 24.1, the highest being 44, the lowest 12; the average age of men was 32.4, the highest being 62 and the lowest 12. The average age of both women and men combined was 26.7. People of all ages progressed uniformly except one of 62 years of age who appreciably lagged behind. The treatment may have, I presume, less effect on patients of advanced age.

Influence of caste.—This series consisted of 16 different castes, the Doms, Oriyas, Mohalis and Telengas predominating; all responded

equally well except the Telengas who were somewhat late in response. These Telengas are primitive in their habits and have a low standard of life.

Iron therapy in anæmia of pregnancy.—Four cases of anæmic pregnant women were treated, two being of the secondary type and two of pernicious type (diagnosed by the necessary hæmatological examination); the former two responded quite well, but the latter two did not. Pernicious anæmia of pregnancy is quite a separate disease which does not respond to iron therapy, so these two cases have not been included in this series.

Relapses.—Relapses after treatment are not uncommon. Five of this series, that is 6.2 per cent. of the cases treated, relapsed, three cases after four months and two cases after three months. So it appears that the effect of treatment on at least a certain proportion of cases is not lasting.

Complications.—Besides constipation two patients complained of abdominal pain, one of anorexia, and another of giddiness. All these complaints were relieved by a brisk saline purge.

Failures.—There were four cases in which response to treatment was unsatisfactory; two were men, aged 62 and 32, respectively, age being possibly the cause in the first case, and two women, aged 18 and 15 respectively; endocrine dysfunction may have been the cause of the failure in the first, and in the second it was almost certainly chronic malaria.

1. ECONOMIC ASPECT OF THE TREATMENT

In table I the average daily dose has been calculated as 87.2 grains, and average time required for treatment as 19.3 days. Therefore the total average amount of iron required in a case is 87.2×19.3 grains, that is $3\frac{1}{2}$ ounces approximately, which costs annas seven only. We know of no other treatment cheaper than this. From the economic standpoint, it may be pointed out that apart from the gain in work, the number of anæmic coolies receiving a special diet has come down from 39 to 5, which is not a negligible saving.

Secondly, along with the disappearance of anæmia the powers of resistance to diseases is likely to be increased. The salutary effect will be noticed mostly in the women coolies who form the bulk of the anæmic patients, and we may expect a diminution in the death rate amongst pregnant women and in the number of marasmic, premature, and still-born babies.

ACKNOWLEDGEMENTS.

I am indebted to my chief, Dr. D. P. Williams, for his valuable instruction in treating these cases and his kind permission to publish the records, and to the manager, Mr. H. O. J. Maxwell, for his unfailing support in this, as in other details of hospital administration. My thanks are also due to my compounder staff for their loyal co-operation in this undertaking.

A NOTE ON THE PREVALENCE OF LEAD POISONING IN INDIA

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It is a melancholy thought to our profession, as Sir James Mackenzie pointed out, that a large percentage of cases of all kinds are never diagnosed. We may take comfort from the fact that a good number of such are cases of lesser ailments, the duration of which does not permit much investigation, but the position would be more serious if a suspicion should arise that major ailments also were escaping us.

There appeared recently in the *British Medical Journal* an article by Professor Bramwell (1931) on the subject of lead poisoning, which might have attracted much attention in this country, since it emphasised the protean character of the manifestations of this disease and should have suggested at least an occasional solution of the complexity of some of the cases with which we have to deal.

The object of this note is to invite the attention of practitioners to the prevalence of lead poisoning in this country. I do not propose to discuss its symptomatology or treatment as these are fully dealt with in all the standard textbooks, but I wish to warn practitioners of the necessity of keeping this disease in mind.

It must be the common experience of those of us who handle many outpatients to meet a large number of cases which defy speedy diagnosis. I will take only two instances, (1) vague abdominal pain, and (2) irregular nervous syndromes.

(1) From time to time cases arrive at hospital with severe abdominal pain and other symptoms suggesting intestinal obstruction. Such cases demand the most anxious consideration as to whether to operate or not, and every faculty is called into play to assist in the decision. Eventually many such cases are left alone, given anti-spasmodics, and the next day they are found to be much better. On the other hand some are operated upon and another successful appendicectomy is added to the list! I suggest that many of these cases are examples of lead colic.

(2) Although cases of nervous disease are common enough, it is curious that only a small number can be labelled with one of the names so common in England. Nearly all the cases seen are cases of atypical combined lesions.

In fact if we were to consider what is the commonest form of recognisable nervous disease we should be forced to say progressive muscular atrophy. Most of us must have seen a number of examples of this disease, and usually atypical in one respect, namely the age of the patient. This view may be compared with the fact that wasting of the hand muscles is one of the typical lesions of lead poisoning.

Examination of the usual type of combined tract lesions has frequently suggested that the case is one of meningo-vascular syphilis, and the evidence of a positive Wassermann reaction may often confirm this view. Further, anti-syphilitic treatment in certain cases produces marked benefit, and there can be no doubt that this type of disease is not uncommon. But a residuum of cases remains, which although they may give a positive Wassermann, do not benefit from treatment, and I suggest that a number of these will be found to be cases of plumbism. Illustrations will be afforded by the cases quoted.

A case of nephritis is also quoted, and confirmation has been found for the textbook statement that urine excretion is often deficient in plumbism. The blue line on the gums, regarded as a classical symptom has not been noted quite as described. It is not usual to find a blue line on the dental margin, but to find blotchy patches on any part of the gums.

If we accept the fact that plumbism is by no means uncommon in India, it is next necessary to consider how the disease is contracted. There can be little doubt that the principal source is from the habit of "tinning" vessels. The tin which is used for this purpose is frequently adulterated with lead. The adulteration may be deliberate, or fortuitous.

The poison may then be conveyed by cooking in such vessels, or by the use of such vessels for storage, particularly of ghee. Ghee kept in tinned vessels may be found to show green spots. These green spots are composed of lead oleate.

This question seems well worthy of the attention of the Indian Research Fund Association.* If these findings can be confirmed independently, legislation might follow which would control an entirely preventable cause of disablement.

A summary of a few cases is appended.

I should like to express my thanks to Drs. Mankad and Fozdar for their energetic co-operation in making these investigations and providing the case summaries, and not least to Mr. J. D. Anklesaria, lecturer on chemistry at this school, who has carried out all the chemical investigations.

Case 1.—A married girl, aged about 20, was admitted in the hospital with 3 or 4 months' history of menorrhagia and metrorrhagia—the bleeding was enough to cause anxiety and was immediately responsible for the patient's seeking of admission to hospital. When admitted she was stated to have been mentally incoherent for a year; she had gradually developed spastic paraplegia, with marked ankle clonus and Babinski's sign for the last eight months and nystagmus, but without any sensory or sphincter trouble. The patient was very pale and had patches of dermatitis on the limbs and trunk.

*The reader's attention is drawn to a paper by Lieutenant-Colonel T. C. Boyd, I.M.S., and Dr. H. D. Ganguly, which appeared in the *Indian Journal of Medical Research* of July, 1932. A résumé of this is given in our 'current topics' section.

While demonstrating the case to the students, disseminated sclerosis, subacute combined degeneration, cerebro-spinal syphilis, progressive muscular atrophy, spinal tumour, and plumbism were considered. The Wassermann reaction was negative and on the grounds of spastic paraplegia, plumbism being excluded, a tentative diagnosis of disseminated sclerosis was made. The demonstrator learnt from the article of Professor Bramwell referred to above that spastic paraplegia could occur in plumbism and he then looked for a blue line on the gum, which was not there. On inquiry the patient was found to have had an abortion 2 years ago and as the pallor and uterine bleeding could not be explained by his diagnosis of disseminated sclerosis, the urine of the patient was examined for lead. Heavy traces of the metal were detected by the chemist, and the diagnosis settled. A little over three months after, the patient left the hospital, walking unsupported though with an element of spasticity, mentally much improved, without any pallor, with a normal skin, and normal menstrual functions.

Case II.—A married male, aged 32, had rather rapidly developed peripheral neuritis without any fever, with a negative Wassermann reaction and without any colic but with a constipation for a few months prior to the neuritis. There was no nystagmus. The neuritis was more of motor than of sensory type though the sensory system was by no means entirely free. While considering the ætiology of the neuritis, lead was thought of. A blue line on the gums was seen easily and the urine was sent for the examination of lead; this was detected. He was treated with sodium thiosulphate intravenously and potassium iodide orally and is on his way to recovery within four months.

Case III.—A married girl, aged about 18, 5 months pregnant, came to the hospital with a badly distended abdomen and the bowels completely locked for 6 days, the coils of the intestines appearing like a ladder under the abdominal wall, there was no vomiting, a clean tongue, a good pulse, and a good general condition. She gave a history of similar attacks for the last ten years, recurring every 6 or 8 weeks and lasting a day or two. She sought admission when she found that the attack had lasted 2 days. In this case the blue line on the gums was searched for and not found. The diagnosis of partial obstruction of the gut was made and the surgeon was summoned in consultation. The latter refused to operate unless vomiting set in or the general condition demanded it, lest premature labour might be precipitated. The patient improved on concentrated magnesium sulphate and hyoseyamus and went home a week later. Next week she was admitted again with signs of uterine bleeding, which ended in a premature delivery. While convalescent from it in the hospital she had again the attack of distension of the abdomen, obstinate constipation, etc. This compelled a urine examination for lead, which was found.

Case IV.—A school boy, aged 12 years, suffered from fever for about 2 months from February 1932, during which time he developed mitral stenosis. In April he attended for low fever and severe dyspnoea. A diagnosis of pericardial effusion was made and was confirmed by x-rays. A partial recovery from it was made by July 1932, when he was seen a second time for oedema all over the left side of the body and left pleural effusion. The oedema soon extended to the right side, but remained always more on the left. There was oliguria and the urine showed much albumen with a trace of sugar, and marked acetonuria. There was definite starvation prior to these symptoms. The diet being limited to a small quantity of boiled milk and very occasionally some bread. The diagnosis of avitaminosis was made by a consultant, and vitamins and a good diet were prescribed. No improvement followed a fortnight's trial. This having been pointed out to the consultant, the latter ordered a urine examination for lead and the report from the chemist showed that this diagnosis was correct.

Case V.—An educated man was going home from work

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A NEW CORNEAL SCRAPER FOR TATTOOING

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TATTOOING of very dense opacities of the cornea for æsthetic as well as for optical purposes is quite an old operation. The material commonly used was Indian ink which was introduced into the deep parts of the cornea with either a grooved tattooing needle or an instrument consisting of a number of fine needles in a handle. The results of this small operation were not always very satisfactory, and in a number of cases the effect did not last very long. To remedy these defects, a new technique was devised by which permanent colouring of the cornea could be effected.

The little operation is done as follows :—

The eye is anæsthetised, preferably with butyn 1 to 2 per cent., instilled twice at an interval of five minutes. Cocaine should be avoided as far as possible on account of its drying and exfoliating effects on the corneal epithelium. The eye is washed with a 1:5000 hydrargyri perchloridum solution and later with sterile distilled water. Saline is not to be used on account of its decomposing effects on the solutions used for tattooing. The next step is to scrape off the superficial corneal epithelium. Ordinary Graefe's knives, secondary knives, scalpels, discission needles, pterygium knives and many other instruments have been used to scrape the cornea, but not being satisfied with any of these instruments, I have devised a special corneal scraper of which an illustration is given herewith. The corneal epithelium is very lightly scraped, particular care being taken to scrape the margins of the opacity. If care is not taken in doing this, the result is a black-coloured central spot with white linings. In scraping the cornea, one has to be very particular in those cases where there is partial anterior staphyloma and the iris lying closely matted with the spurious cornea; if care is not taken here, the resulting uveitis may be so

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one evening, after a period of heavy strain, when he fell down in the road and became 'unconscious'. He remained 'unconscious' for three days after which he was brought to Ahmedabad. When seen he was mentally confused, cerebation was very slow, paraplegia was present and he could not sit up; paræsthesia was noted but this might have been an association of the mental confusion. Blue patches were found on the gums and a diagnosis of lead encephalopathy with other evidence of plumbism was made and confirmed by urinary analysis.

The patient rapidly improved, and could walk with assistance within ten days.

REFERENCE

Bramwell, E. (1931). Some Clinical Pictures Attributable to Lead Poisoning. *Brit. Med. Journ.*, Vol. II, p. 87.

as a case of sandfly fever, and developed severe vomiting and restlessness after 2 days. There was no change in breath sounds and no dullness on examination of the lungs. On blood examination, no malaria parasites were found and there was no leucocytosis. Crepitations at the bases of both lungs previously present were still audible after 4 days; urine examination revealed a large amount of urobilin; when he was treated as a case of malaria, with quinine, he was completely freed from all symptoms within two days.

Case 2.—The patient, a teacher, was reported to be suffering from severe dysentery and temperature of 100° to 101°F. for 2 days. On examination he was found collapsed with cold clammy sweat and a feeble pulse. He passed about 20 ounces of blood in the stools on two occasions during the day. There was a frequent tendency to vomiting; the spleen was just palpable. There was no mucus in the stools, the urine was found full of urobilin, and blood films full of malignant tertian malaria parasites; he was treated as a case of malaria fever and had no recurrence of blood in the stools or of vomiting.

The vomiting tendency as in the previous case suggested malarial infection; urobilin in the urine and the blood findings confirmed it.

Choleraic symptoms in malarial infections are frequent, but the passage of pure blood in the stools is very infrequent; the case is therefore interesting on this account.

Case 3.—An Anglo-Indian, employed in a European firm, suffered from hæmaturia and slight fever. Blood culture was negative. No definite diagnosis was made as the patient recovered after 36 hours' illness. Ten days later he developed symptoms of acute dysentery and passed about 40 stools full of blood, in the course of a few hours. His temperature was 104°F. Malaria parasites were found in his blood and urobilin in the urine. He was treated with quinine and recovered quickly.

Case 4.—A young man of 28 years, with a history of attacks of biliary colic and an enlarged tender gall bladder suggesting cholecystitis and cholelithiasis; urine examination showed the presence of a large amount of urobilin and a skiagram after Shadocel confirmed the presence of stones in the gall bladder.

Cases of cholecystitis on account of the associated cholangitis also show an increased amount of urobilin, and the presence of urobilin in cases of cholecystitis is sometimes of diagnostic value.

In three cases of cholecystitis and cholelithiasis, diagnosed by symptoms and confirmed by x-rays, a large amount of urobilin was present.

In 11 cases in this series where the blood films showed malaria parasites and urobilin was absent in the urine, some were afebrile and possibly blood destruction was not marked; in others the temperature was present for only a few hours, when the blood films were examined, and urobilin had not yet appeared in the urine. There were, however, four cases where fever was present for three to four days, and showed malaria parasites without the presence of urobilin in the urine. Such cases are exceptional and difficult to explain.

In 20 cases, where malaria parasites were found in the blood films and urobilin was present, estimation of urobilin in the specimens of urine submitted was done by the following

method, as recommended by Elman and McMaster (1925) and modified by the writers in the expression of results.

A standard solution of acriflavine containing 1 milligramme of acriflavine dissolved in 30,000 c.cm. of distilled water, representing 1 unit (equivalent to 1 milligramme of urobilin dissolved in 950 c.cm. of the standard diluent) was prepared and the urobilin estimated as follows:—

Take 10 c.cm. of urine; add 1 drop of Lugol's iodine solution and 10 c.cm. of saturated solution of zinc acetate in absolute alcohol, filter through filter paper and compare with standard solution. It is best to prepare a stock solution of acriflavine containing 10 milligrammes of acriflavine in 1,000 c.cm. distilled water and from this to prepare standard solutions by diluting 1 c.cm. of this stock solution in 50 c.cm. distilled water and 1 c.cm. of the stock solution in 100 c.cm. distilled water, representing 6 units and 3 units of urobilin, respectively. It is advisable to use test tubes with a length of 10 inches and a bore of $\frac{1}{2}$ inch. These tubes may previously be marked with a glass pencil to represent volumes of 5 c.cm. Comparison is best made in a tropical country in direct sunlight using a Cole comparator, with the light falling on top of the liquid through the open end of the test tubes. Amounts varying from 0.01 to 0.5 or 1 c.cm. of the filtrate were taken, diluted with the following diluting fluid up to the 5 c.cm. mark.

Composition of the diluting fluid

Sixty per cent. alcohol—1,000 c.cm., zinc acetate—25 gr., concentrated hydrochloric acid 1 c.cm. filtered, repeated till perfectly clear.

Standard solutions representing 3 units and 6 units, respectively, were placed in adjacent compartments of the Cole comparator with the diluted filtrate in the middle compartment and the result compared.

Gradually increasing amounts of the filtrate were added to the middle tube containing the diluted filtrate to make the colour match first with the three-units tube and then the six-units tube.

Suppose 0.01 c.cm. of the filtrate diluted to 5 c.cm. matched with the standard representing 3 units; the number of units in the filtrate is $\frac{3 \times 5}{0.01}$ or 1,500 units, and, since the urine had been originally diluted with an equal amount of reagent, it will have 3,000 units. In this estimation the precipitate produced is neglected. It is a rough and ready method of finding the amount of urobilin in urine.

Calculated in this way, urobilin units varied within very wide limits, therefore no hard and fast limit could be laid down as to the presence

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LIFE TABLES FOR BENGAL, WITH NOTES ON THE METHOD OF PREPARATION OF LIFE TABLES

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ONE way of expressing the death rates experienced by a population in a given period of time is by means of a 'life table'. This gives a concise yet comprehensive table of survivorships up to any given age, and the prospective duration of life from that age onwards. A life table facilitates comparison between different places and between different periods as regards the expectation of life of the populations. Further, an exact statement of the average duration of human life from birth or from any subsequent age can only be given by the means of the life-table method. Life tables, however, do not actually trace the same persons throughout life, but assume that a given number of persons are subjected throughout the whole of their lives to the death rates of a given group of years.

Thus we see that a life table can be used in a number of ways. It supplies the information regarding the probability of living or dying at each age. Next it gives the probability of surviving 5, 10, 15 years and so on. Then again we can ascertain the number of survivors out of, say, 10,000 children at the end of each year of life, until the whole number becomes extinct

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of urobilin units before a patient could definitely be diagnosed as one of malarial fever. However, the greater the amount of urobilin the greater the suspicion of malaria infection in a febrile case.

Tests to detect the presence of urobilin in urine were the same, as were given in the *Indian Medical Gazette*, May, 1931, p. 241.

Summary

I. Four important conditions in the tropics, particularly in the Punjab, in which urobilin is present in large amount are in order of importance—malaria fever, lobar pneumonia in the resolution stage, internal hæmorrhage, and cholecystitis.

II. The presence of a large amount of urobilin in the urine differentiates cholecystitis from kidney lesions, appendicitis and other abdominal conditions.

III. The condition in which urobilin is present in the largest amounts is malaria infection.

All the members of the pathology department, King Edward Medical College, worked together in this investigation.

REFERENCE

Elman, R., and McMaster, P. D. (1925). *Journ. Exper. Med.*, Vol. XLI, p. 503.

by death, and lastly the table enables us to estimate the expectation of life at the end of each year of life. The last two supply composite information regarding the average past and average future. It is needless to point out how valuable this information is, not only for students of public health, but also for insurance companies.

Now a life table can be constructed by tracing the lives of a number of children from birth to death, but if followed in practice this method would be of no real value, as the table when completed would be out of date. The alternative method, the method commonly used, requires that we should ascertain the population and the deaths for each year of life; this is the method which the writer has actually adopted here. There is a third method, that is, by actually tracing the lives of a selected group for a certain number of years, as is done in insurance practice.

The life table has six important columns, $P_x, d_x, q_x, p_x, l_x, o_{ex}$. To construct a life table only one piece of information is needed and that is the 'rate of mortality'. The expression 'rate of mortality' is used technically to denote the ratio, represented symbolically by q_x , of the number of deaths in a particular age group, x to $x + 1$ years, to the number of persons entering upon that year of age. The successive values of q_x can be derived by means

of the formula $q_x = \frac{d_x}{P_x + \frac{1}{2}d_x}$, where d_x represents

the average number of deaths of persons of ages between x and $x + 1$ years, per annum, and P_x the average number of persons enumerated at the census as having been aged x at their last birthday, i.e., persons aged between x and $x + 1$. Therefore the number of persons aged x exactly is the number of the census population, i.e., P_x plus the number of deaths occurring in the first half of the year, i.e., $\frac{1}{2}d_x$. Thus, the rate of mortality depends on two things d_x and P_x .

Now the values of d_x , the average number of deaths at each year of age in a given population, can be ascertained from the government annual reports of vital statistics, and those of P_x , the number of persons of each sex at each last birthday, can be ascertained from the census report.

The basis of the investigation having been thus determined, it becomes easy to obtain directly from the data a measure of the mortality experienced in the country during the period at each age by means of the ratio already mentioned, i.e.,

$q_x = \frac{d_x}{P_x + \frac{1}{2}d_x}$, from which the factor, p_x , can easily be calculated by $p_x = 1 - q_x$. Having ascertained p_x , the number living at each age (l_x) is obtained by multiplying the

*For definitions see list at end of paper.

number living at the immediately preceding age by p_x , e.g., $l_x = l_{x-1} \times p_x$.

The final column O_{ex} , known as the 'complete expectation of life', is the average number of years lived (subsequently) by persons who reach the age of exactly x years. The value is determined by the equation $O_{ex} = \frac{x+1 + l_{x+2} + l_{x+3} + \dots + l_{x+(n-x)} + \frac{1}{2}}{l_x}$

years. Now in the case of Bengal n is 90, which is the maximum age lived in this province. The values of the series $l_{x+1} + l_{x+2} + \dots$ cannot be obtained unless we calculate all the values right up to the last figure, $l_x + (n-x)$, or l_{90} in the case of Bengal, and work backwards; the whole series, $l_{x+1} + l_{x+2} + \dots$, can be symbolized by T_x , the various values of which are shown in a column in the tables III (a) and III (b). The T_x for each age is thus obtained by adding the figures in the l_x column up as far as the year in question, e.g., in table III (a), $7 + 13 = 20$, $7 + 13 + 21$ (or $20 + 21$) = 41, $41 + 32 = 73$, etc., so that $T_x = l_x + T_{x+1}$.

O_{ex} thus equals $\frac{T_x}{l_x} + \frac{1}{2}$ years.

Criteria for comparison

The criteria adopted for the comparison of the life tables of different epochs and different places are as follows:—

- (1) At a selected age, the probability of dying before some later age is reached.
- (2) The number of survivors at a selected age out of a stated number of births.
- (3) The expectation of life at birth, or at some selected age.
- (4) At some selected age, the probability of surviving an indicated number of years, say 10 years.

Some authorities on the subject of life tables consider that (4), of which (1) may be regarded as a corollary, is the best criterion of the characteristic of a mortality experience, though the expectation of life at birth provides a comprehensive figure, which summarizes the whole table, and is the figure most often quoted to indicate the state of health of a population.

It is clear that 'the expectation of life' has but a 'mean' value and, like every other case of a mean value, it suffers from the defect that it gives no information of the dispersion round the mean. For instance, to state that the average height of an Indian government servant is 5 feet, gives a good indication of the height of each individual, but to say that their average pay is Rs. 40 gives little indication either of the pay of sweepers in Writers' Building or the pay of a Member of Council; in the former case the dispersion round the mean is small, whereas in the latter it is very large.

Examples

- (1) At the age of 20 years, what are the respective chances of a Bengali male and a Bengali female surviving to the age of 40 years?

From the l_x columns of tables IV (a) and IV (b) the numbers of the survivors at the age of 20 and at the age of 40 can be seen; they are 4,432 and 2,910 for males, and 5,035 and 3,296 for females. The chances of survival are, therefore,

$\frac{2910}{4432} = 0.6565$ for males, and $\frac{3296}{5035} = 0.6546$ for females and the chances of dying are thus, $1 - 0.6565 = 0.3435$, and $1 - 0.6546 = 0.3454$.

(2) Out of 1,000 births how many males survive to the age of 20 years?

Again column l_x gives the number of survivors at this age out of 10,000 births, namely 4,432. The number of survivors out of 1,000 is therefore 443.2.

(3) How long may a man who has reached the age of 20 years expect to live?

This figure is taken directly from the O_{ex} column; it is 29.43 years, that is, he will probably live to the age of (20 + 29.43 or) 49.

Life table for Bengal

Hitherto only two life tables for Bengal have been published—one on the population basis of 1891–1901, and another on that of 1901–1911. The late T. G. Ackland, the celebrated actuary, was responsible for both of them. No life table has been constructed for the last 20 years. This is a very undesirable state of affairs in view of the growing importance of the subject. The data on which life tables are constructed in this country are often not very dependable on account of the omissions and misstatements that are to be found in them. These errors can be adjusted by the process known as 'graduation'. Here only the method by which the present table was constructed will be discussed.

In the *National Life Tables of England and Wales* we find that to construct a life table one should know the population living or dying in each year of life, but often we only know the population and the deaths in wider age groups, e.g., 0–5, 5–10, 10–15, and not at each year of life. In such cases we must reach the value for each year of life by some method of interpolation (mathematical or graphical). Having by some such method reached our population and deaths at each year of life, we can determine the probability of dying or living at any age by the methods already discussed.

To find out the population at each age (P_x), we have based our calculation on the census figures of 1921, using the groups 0–1, 1–5, 5–10, 10–15, 15–20, 20–30, 30–40, 40–50, 50–60, and 60 and up, years.

In order to arrive at d_x , the deaths at each age, we have taken the figures of deaths from the annual reports of deaths of the year 1920, 1921 and 1922 (see table I) and have calculated the average of these three years as representing the death rate of 1921, for each of the age groups 0–1, 1–5, etc.

To find out the rate of mortality of each group (q_x), we have used the formula $q_x =$

$\frac{d_x}{p_x + \frac{1}{2} d_x}$ where d_x etc., applies to the larger

groups (e.g., 1-5, 5-10, etc.), as d_x etc., applied to each individual year (see table II). To find out p_x , we have deducted the values of q_x from 1.

Then the succeeding values of p_x for each age have been determined by graphical methods of interpolation, and from these q_x and l_x can be calculated by the methods already described above, i.e., by using the formula $q_x + p_x = 1$, and $l_{x-1} \times p_x = l_x$.

The final column ($O_{e,x}$), the complete expectation of life, has been obtained from the column T_x , which represents the sum of number of years lived by the persons who reach age x , as explained above, from the equation $O_{e,x} = \frac{T_x}{l_x} + \frac{1}{2}$ years.

To obtain the values for the years of age under 5, we should not utilise the census population, because it has been shown that, though the total population under 5 may be correct, the population under each individual year of age cannot possibly be correct. To obtain the population of these individual ages the returns of births and deaths are utilised. Knowing the births for the 5 years previous to the census and the deaths at ages under 5 for the same year, we can calculate the population at individual ages at the census time; this is what is actually done in English life tables.

In our present table we have taken the mean of the total births of 1920, 1921 and 1922, and that has been taken as the population between 0 and 1. For the rest we have taken the census figures only. We know at age 0 to 1 it is inaccurate to assume that half the deaths take place in the first six months of life and half the deaths in the second six months. The proportion is rather 70 to 30—so instead of taking $\frac{1}{2} d_x$ to obtain q_x for age 0, we have taken $\frac{7}{10} d_x$. No great error will be introduced by taking $\frac{1}{2} d_x$ at the other ages.

Conclusion

Resting as it does on incorrect data, though the only data available, the present table has only a limited value, but it will provide important material for comparison which should convey sound impressions regarding the value of progressive policies in respect of sanitation, education, etc., to medical men and welfare workers that are not themselves thoroughly conversant with statistical methods.

The different functions used are summarised for easy reference:—

- l_x = the number of persons surviving at the exact age x years.
- d_x = the deaths in the year of age x to $x + 1$ among the persons, who enter on that year.
- p_x = the probability of a person aged x living a year.
- q_x = the probability of a person aged x dying within a year.
- $O_{e,x}$ = the complete 'expectation of life' or the total future life time, which on the average will be passed through by a person aged exactly x .
- T_x = the sum of the number of years lived (subsequently) by all the persons reaching the age x .

REFERENCES

- Ackland, T. G. (1913). Age Distribution of the Indian Population and the Estimated Rates of Mortality. *Journ. Inst. Actuaries*, Vol. XLVII, p. 315.
- Chaudhuri, H. P. (1932). All India Life Tables. *Indian Journ. Med. Res.*, Vol. XX, p. 585.
- Meikle, H. G. W. (1926). Report on the Age Distribution and Rates of Mortality deduced from the Indian Census Returns of 1921 and previous enumerations. Calcutta: Government of India, Central Publication Branch.
- Thompson, W. H. (1923). *Census of India, 1921*, Vol. V. Bengal, Parts I and II. Calcutta: Bengal Secretariat Book Depot.
- Watson, A. W. (1927). Report on Life Tables. Registrar-General's Decennial Supplement. England and Wales, 1921, Part I.
- Watson, A. W. (1927). Annual Reports of the Director of Public Health, Bengal, for the years, 1920, 1921 and 1922. Calcutta: Bengal Secretariat Book Depot.

TABLE I (a)
Deaths of males

	0-1	1-5	5-10	10-15	15-20
1920 ..	132,656	95,835	65,618	38,479	39,704
1921 ..	142,637	89,778	63,245	38,017	37,700
1922 ..	129,447	75,457	52,057	32,865	32,204
Total ..	404,740	261,070	180,920	109,361	109,608
Average ..	134,913	87,023	60,307	36,457	36,536
Population	697,706	(1-2) (2-3) (3-4) (4-5) 292,676+596,010+693,811+696,135 2,278,832	3,801,542	2,070,434	2,206,286
Central death rate.	193.366	38.187	15.863	11.873	16.560

TABLE I (a)—*concl'd*

	20-30		30-40		40-50		50-60		60+up		
1920 ..	85,527		87,886		69,353		56,638		87,363		
1921 ..	80,088		81,897		66,660		54,320		81,996		
1922 ..	66,261		67,177		55,034		44,865		68,937		
Total ..	231,876		236,960		191,047		155,823		238,501		
Average ..	77,292		75,987		63,682		51,941		79,500		
	(20-25) (25-30)		(30-35) (35-40)		(40-45) (45-50)		(50-55) (55-60)		(60-65) (65-70) (70+up)		
Population	1,951,336+2,351,199		1,980,264+1,677,492		1,421,746+945,598		862,545+409,472		476,464+160,766+336,676		
	4,482,537		3,657,756		2,367,344		1,272,015		973,906		
Central death rate.	17.242		21.594		26.900		40.833		81.630		

TABLE I (b)
Deaths of females

	0-1	1-5				5-10	10-15	15-20
1920 ..	132,656	93,744				54,911	28,079	47,927
1921 ..	125,525	87,918				52,147	27,660	46,552
1922 ..	110,004	71,225				42,062	23,789	38,931
Total ..	368,185	252,887				149,120	79,528	133,410
Average ..	122,928	84,296				49,707	26,509	44,470
		(1-2)	(2-3)	(3-4)	(4-5)			
Population	705,587	303,698+647,977+771,195+718,922				3,686,676	2,368,178	2,380,614
		2,441,792						
Central death rate.	173.937	34.522				13.482	11.193	18.660

	20-30	30-40	40-50	50-60	60+up
1920 ..	101,927	72,494	46,487	46,407	77,018
1921 ..	95,454	67,002	44,209	44,209	72,404
1922 ..	77,632	54,226	38,494	38,494	57,740
Total ..	275,013	193,722	129,390	129,390	207,162
Average ..	91,671	64,674	43,130	43,130	65,721
Population	2,232,197+2,217,269	1,710,569+1,234,894	1,169,887+693,413	794,647+341,922	511,021+148,633+326,862
	4,449,466	2,945,462	1,863,300	1,136,569	986,518
Central death rate.	20.602	21.957	24.600	37.946	66.190

TABLE II (a)

Males

Ages	Actual deaths d_X	Census population in the age groups P_X	Population at age x $P_X + \frac{1}{2}d_X$	Rate of mortality q_X	Probability of living p_X
0	134,913			0.2107	0.7893
1	87,023	2,278,832	2,322,344	0.0368	0.9632
5	60,307	3,801,542	3,831,696	0.0157	0.9843
10	36,457	3,070,434	3,088,782	0.0118	0.9882
15	36,536	2,206,286	2,224,554	0.0163	0.9837
20	77,292	4,482,537	4,521,183	0.0170	0.9830
30	75,987	3,657,756	3,695,758	0.0204	0.9796
40	63,682	2,367,344	2,399,185	0.0262	0.9738
50	51,941	1,272,015	129,786	0.0393	0.9607
60	79,500	973,906	1,013,656	0.0755	0.9245
70+up					

TABLE II (b)

Females

Ages	Deaths (actual) d_x	Census population in the age groups P_x	Population at age x $P_x + \frac{1}{2}d_x$	Rate of mortality q_x	Probability of living p_x
0	122,728	705,587		0.2063	0.7937
1	84,296	2,441,792	2,483,940	0.0334	0.9666
5	49,707	3,686,676	3,717,530	0.0134	0.9866
10	26,509	2,368,178	2,381,433	0.0111	0.9889
15	44,470	2,380,614	2,402,849	0.0184	0.9816
20	91,671	4,449,466	4,495,302	0.0202	0.9798
30	64,674	2,945,402	2,977,739	0.0215	0.9785
40	45,837	1,863,300	1,886,219	0.0241	0.9759
50	43,130	1,136,569	1,158,134	0.0336	0.9634
60	65,721	9,865,161	1,019,377	0.0625	0.9375
70+up					

TABLE III

Births		Males	Females
1920	..	702,666	657,247
1921	..	674,791	626,210
1922	..	664,469	611,145
Total	..	2,041,926	1,894,602
Average	..	680.679	631,534
Deaths	..	134,913	122,728
Population (0-1).		545,766	508,806
Population at age 0.		$545,766 + \frac{1}{2} \times 134,913$ or 640,287	$508,806 + \frac{1}{2} \times 122,728$ or 5,947,156
Rate of mortal- ity (0-1).		210.71	206.30
Infant mortal- ity.		198.20	194.30

TABLE IV (a)
Bengal life table (males)

Ages	l_x	d_x	p_x	q_x	T_x	O_{ex}
0	10,000	2,107	0.7893	0.2107	230,981	23.59
1	7,893	1,175	0.8512	0.1488	223,088	28.76
2	6,718	558	0.9092	0.0928	216,170	32.70
3	6,160	380	0.9353	0.0647	210,010	34.59
4	5,780	206	0.9630	0.0370	204,230	35.83
5	5,574	176	0.9684	0.0366	198,656	36.13
6	5,398	121	0.9738	0.0262	193,258	36.32
7	5,267	110	0.9791	0.0209	187,991	36.19
8	5,157	81	0.9843	0.0157	182,834	35.95
9	5,076	75	0.9854	0.0146	177,758	35.51

TABLE IV (b)—concl'd

Ages	l_x	d_x	p_x	q_x	T_x	O_{ex}
53	2,325	79	0.9661	0.0339	31,988	14.25
54	2,246	79	0.9655	0.0345	29,742	13.74
55	2,169	80	0.9631	0.0369	27,573	13.21
56	2,089	82	0.9606	0.0394	25,484	12.69
57	2,007	86	0.9600	0.0400	23,477	12.19
58	1,921	89	0.9570	0.0430	21,556	11.72
59	1,832	85	0.9537	0.0463	19,724	11.26
60	1,747	87	0.9502	0.0498	17,977	10.79
61	1,660	85	0.9491	0.0589	16,317	10.32
62	1,573	87	0.9449	0.0551	14,742	9.86
63	1,488	84	0.9438	0.0562	13,254	9.40
64	1,404	86	0.9389	0.0611	11,850	8.94
65	1,318	83	0.9375	0.0625	10,532	8.49
66	1,235	84	0.9318	0.0682	9,297	8.02
67	1,151	87	0.9246	0.0754	8,146	7.57
68	1,064	89	0.9166	0.0834	7,082	7.15
69	975	91	0.9074	0.0926	6,107	6.76
70	884	93	0.8955	0.1045	5,223	6.40
71	791	87	0.8906	0.1094	4,432	6.10
72	704	82	0.8849	0.1151	3,728	5.79
73	623	75	0.8811	0.1189	3,005	5.48
74	548	74	0.8651	0.1341	2,557	5.16
75	474	67	0.8589	0.1411	2,083	4.89
76	407	62	0.8484	0.1516	1,676	4.69
77	345	54	0.8448	0.1552	1,331	4.35
78	291	48	0.8367	0.1633	1,040	4.07
79	243	42	0.8292	0.1708	797	4.79
80	201	36	0.8235	0.1765	596	3.46
81	165	31	0.8150	0.1850	431	3.11
82	134	27	0.8000	0.2000	297	2.71
83	107	23	0.7857	0.2243	190	2.27
84	84	28	0.6777	0.3223	106	1.76
85	56	22	0.5764	0.4236	50	1.39
86	33	16	0.5384	0.4616	17	1.01
+ up	17	17				

A Mirror of Hospital Practice

REPORT ON A CASE OF TUBERCULAR IRITIS

By E. O'G. KIRWAN, F.R.C.S.I.

LIEUTENANT-COLONEL, I.M.S.

Professor of Ophthalmology, Medical College, Calcutta

Miss A. D., Bengali girl, age 16 years. Height—5 feet. Weight—6 stones 5 pounds.

Complaint.—Patient came to the Eye Infirmary, Medical College, on the 1st June, 1932, complaining of pain and blurring of vision for about three weeks. The left eye only was affected.

Past history.—There was no history of any previous serious illness but the family history was interesting in the fact that her grandfather died of tuberculosis of the lungs in 1911. Her elder sister died of tuberculosis of the lungs at the age of 11 years about 8 years back. Her grandmother died of tuberculosis of the lungs 4 months back.

Present examination.—The vision in the right eye is 6/6. The left eye is 6/18. The cornea is not involved. The iris shows no acute inflammation, there are some bands of posterior synechiae, and isolated spots of pigment on the anterior capsule of the lens. There are numerous small grey nodules to be seen scattered over the anterior surface of the iris, some at the pupillary margin, some on the collarette, and some at the ciliary margin of the iris. These can be seen in Plate II, which

shows the iris under the corneal microscope and slit lamp.

Diagnosis.—Tubercular iritis. The von Pirquet test is positive. Clinically nothing abnormal can be found in the lungs. X-ray examination shows early infiltration in the right apex and subapical region.

The patient was kept under observation without any local or general treatment for a week after admission into hospital and during this period there was definite increase in the number of nodules. For the past three weeks she has been under local treatment as well as general and her ocular condition has improved, there has been no increase in the nodules and some have diminished in size.

Tubercular iritis whilst common in Europe and America is very uncommon in India. At the Eye Infirmary, Calcutta, we only see very few cases of ocular tuberculosis in the year, yet tuberculosis of the lungs in Calcutta is common. Syphilitic iritis is common and by far the commonest cause of iritis in Calcutta. Tubercular nodules resemble syphilitic nodules but are more numerous, are grey in appearance and do not change colour. They are also scattered irregularly on the surface of the iris. Syphilitic nodules are about the size of a pin's head, are reddish-yellow in colour and as they become vascularised, change colour to a muddy brown. Syphilitic nodules are always situated at the outer or inner margins of the iris, never between.

(Continued at foot of opposite page)

PLATE II



Tubercular Iritis.

THE OCCURRENCE OF HÆMOGLOBINURIA DURING TREATMENT OF MALARIAL FEVER WITH ATEBRIN AND PLASMOQUINE

By N. G. BANERJEE, M.B.

and

PHANINDRANATH BRAHMACHARI, M.Sc., M.B.
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THE following case is published not with the idea of showing any causal relationship between the development of hæmoglobinuria and the combined administration of atebtrin with plasmoquine, but to point out that these drugs failed to avert an attack of hæmoglobinuria in the patient during their administration.

(1) Patient, B. K. M., had an attack of fever with severe rigors in the third week of last September while staying at the Sunderbans. He was treated with quinine sulphate which was continued up to 1st October. On this day he had another attack of fever with rigors. He then came under the treatment of one of us (N. G. B.) and was given three successive injections of five grains of quinine bihydrochloride after which the fever stopped. He had another attack of fever about ten days after the second, and was again treated with intramuscular injection of quinine bihydrochloride. After four days, he was free from fever and no further quinine was administered to him.

He was put on combined treatment of atebtrin and plasmoquine, two tablets of each being given per day. This was continued for five days. On the fifth day of treatment, he again had fever followed by jaundice and hæmoglobinuria. Next day, he had intense jaundice, the liver was enlarged and tender. There were very marked hæmoglobinuria, severe prostration and some amount of difficulty in breathing. Altogether 15 tablets of atebtrin (gr. $1\frac{1}{2}$ each) and ten of plasmoquine (gr. $\frac{1}{2}$ each) were given to the patient. As soon as hæmoglobinuria appeared, these drugs were stopped. The attack lasted for three days. The patient recovered and is under the observation of one of us (N. G. B.).

During the attack of hæmoglobinuria, the patient was treated with cholesterin, adrenalin chloride, alkalies, and intravenous injection of calcium chloride.

Blood examination—

3-11-32. Red blood cells 2,280,000; Hæmoglobin—32 per cent.; no malarial parasites found.

10-12-32. Red blood cell 3,910,000; Hæmoglobin 60 per cent.

The reticulocyte count was made by one of us (P. N. B.) and is given below:—

3-11-32.	Reticulocyte percentage	.. 7.2
5-11-32.	Ditto.	.. 4.92
10-12-32.	Ditto.	.. 4

(Continued from previous page)

Tubercular iritis is as a rule to be found in association with some latent tubercular affection of the lungs, whether active or cured, as evidenced by calcareous foci at the hilus, fibrous bands, etc.

Treatment.—The treatment of ocular tuberculosis is divided into the general invigorating treatment and the complete local treatment of the eye.

(1) Climatic and constitutional treatment in the mountains.

(2) Tuberculin treatment—Incipient dose small, beginning with (1/100,000 mg.) and increasing up to (1/1000 mg.). The interval between the doses being from 4 to 8 days.

(3) Light therapy by Finsen light or better Röntgen raying with frequently graduated doses.

(4) Subconjunctival sodium chloride injections from 1 to 4 per cent. once or twice a week.

The following points are noticeable in the present case—

- (1) No hæmoglobinuria developed when patient was having treatment with quinine.
- (2) An attack of hæmoglobinuria took place when patient was being treated with atebtrin and plasmoquine.
- (3) The administration of the above drugs failed to avert an attack of hæmoglobinuria.

A CASE OF ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS

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A PARSİ girl aged 12 was admitted for an eruption over the nose, cheeks and palms; fever and cough.



Origin, duration and progress of the disease.—The present complaint started about 1½ months back. The patient used to get (as she described) low fever intermittent in character. Along with this there was general weakness and lassitude. About a fortnight back she noticed erythematous patches over both cheeks. In spite of treatment, the eruption increased and new patches also appeared forming the typical butterfly or bat's-wing patch across the face.

report the following case, treated with that drug :—

Case record.—On 20th October, a Mahar woman, aged about 20, primipara, was admitted to this dispensary, with a transverse presentation. Under chloroform anaesthesia, internal version was done and the child extracted. The placenta and its membranes came away in about ten minutes. There was no post-partum haemorrhage. Since the day of operation, she began to run a temperature with rigors, ranging between 101° to 106°F. Lochial discharge was first normal but later on it became scanty and foul-smelling. The uterus was tender and there was a hard tender mass in the right iliac fossa.

Treatment.—Hot vaginal douche (iodine) every morning. Cinchona mixture containing strychnine and ergot was prescribed for the first two days for which an alkaline diaphoretic mixture was substituted later. She was given three intravenous iodine injections (21st, 22nd, and 23rd October) two intramuscular injections of quinine on 24th and 25th October, and two intravenous injections of mercuriodrome 1 c.cm. of a 1 per cent. solution in 5 c.cm. of sterile water on 27th and 28th October without the slightest effect on her temperature. On the morning of 29th October her uterus was lightly curetted with a dull flushing curette and her temperature went up to 106°F. in the evening. Her pulse, which had hitherto been below 100, increased to 140 per minute and she became restless. I then resolved to try hydrochloric acid injections. Accordingly I prepared the requisite solution and injected 5 c.cm. of it intravenously at about 5 p.m. The effect was dramatic. Within about three hours, her temperature dropped down to 101°F. and she was normal next morning and remained so until her discharge. The hard tender mass in the right iliac fossa and tenderness of the uterus also disappeared after three more injections.

Dr. Burr Ferguson of Birmingham, Alabama, has advocated the use of hydrochloric acid in the treatment of all manner of infections. The dose recommended is 10 c.cm. of a 1:1500 solution of hydrochloric acid. Injections should be given either intramuscularly or intravenously, daily or two to three times in a week according to requirements of a case.

SYPHILIS OF THE BRAIN*

By D. B. BHATE, L.M.F. (C. P.)

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On 14th November, 1932, I saw a patient who was reported to be getting fever for the last two weeks, every afternoon, with rigor. The history was that the patient was unconscious till the next morning, when the temperature used to go down. But since 12th November, 1932, the patient did not regain consciousness though his morning temperature was normal.

He was a male of about 35 years and when I saw him he was in a state of muttering delirium, temperature was 103°F., pulse—130 per minute, respirations—30 per minute, lungs and heart—normal, liver and spleen—not palpable. His bowels were constipated and I gave him a soap-and-water enema, and suspecting it to be a case of cerebral malaria I gave an intramuscular injection of 10 grains of quinine with a diaphoretic mixture every third hour. Next morning the temperature was 97°F., and pulse—100 per minute,

respiration—20 per minute, other conditions being exactly the same, quinine and arsenic mixture 1 oz. every fourth hour was given. Bowels were clear and glucose water with milk and chicken soup occasionally was prescribed as the diet. The patient retained two doses of the mixture but the third and fourth doses were vomited and everything that was administered thereafter was vomited. In the evening the temperature in spite of the quinine mixture rose up again to 100°F.

On 16th morning the temperature was 96°F., pulse—98 per minute, and the patient was in the same condition tossing his head to and fro and in the same state of delirium. Urine was passed into the bed. A carminative mixture with brandy as a stimulant, alternating with euquinine powders, were prescribed for the day. Temperature rose in the evening to 100°F. Since the bowels did not move a glycerin enema was given and another injection of quinine was administered. At night a hypnotic was prescribed.

On the 17th his condition was unchanged. Blood and urine examinations revealed no abnormality.

It was not possible to obtain a definite history, but on the chance of the disease being of syphilitic origin an injection of acetylarsan, three cubic centimetres intramuscularly, was given on the evening of the 18th.

The patient had a good sleep that night and next morning he was looking better and he regained consciousness.

He was then given a mixture of potassium iodide and liquor hydrargyri perchloridi every six hours with marked benefit, so the injection and mixture were continued.

On recovery of consciousness the patient gave a history of syphilis five years previously.

It was not possible to have a Wassermann test done to confirm the diagnosis.

Special Articles

TROPICAL GYNÆCOLOGY AND OBSTETRICS

(A POST-GRADUATE CLINICAL LECTURE)

By V. B. GREEN-ARMYTAGE, M.D.,

F.R.C.P. (Lond.), F.C.O.G.

LIEUTENANT-COLONEL, I.M.S.

Professor of Midwifery and Gynaecology, Calcutta Medical College, and Surgeon to the Eden Hospital for Women, Calcutta

In 1928 I published a plea for vaginal hysterectomy and detailed 150 cases in which this operation had been performed. Since then I have done in this hospital a further series of 136 with one death only. For some reason vaginal hysterectomy is dreaded by gynaecologists in India, and yet there can be little doubt that it has a peculiar attraction for women in the tropics, who will readily face and endure anything that can be performed from below rather than per abdomen.

Doyen, the great French surgeon, used to state, and I have myself heard him, 'that no man should call himself a gynaecologist who cannot perform a vaginal hysterectomy in private'. I think there is a good deal of truth in this for surgeons who are quite amiable in the valleys and dales of the abdomen tremble when working anatomically.

* Rearranged by Editor.

vaginam, for they are unable to visualize up side down. And yet there is really no need to be afraid, tissues are cut, vessels are tied and fascial planes are opened, exactly as one would do if performing a complete hysterectomy from above.

To my mind, fibroids, unless in very fat or debilitated patients, are better treated by operation than by radium, for radium has suffered the fate of every other new remedy in the tropics, in that it has been used indiscriminately without regard to pathology and clinical symptoms, with the result that, in some, intense inflammatory reaction has occurred; in others, where adenomyomata existed, bleeding, growth, and pain increased; in a few, sloughing, accompanied by a stinking discharge has continued for months.

In the tropics of both hemispheres, fibromata of the uterus are extremely frequent and make up some ten per cent. of all operations. They are found in the multipara as often as in the nullipara, and cause much hæmorrhage and invalidism. Provided they are not bigger than a 3-months' pregnancy in a large proportion of cases they can be removed vaginally, provided the surgeon is accurate and fearless in his diagnosis and technique. In a small percentage there may be slight old salpingitis or adhesions between the pelvic wall, but never yet have I found difficulty in separating these adhesions, or been prohibited from finishing any operation vaginally, and compelled to open the abdomen.

Scores of post-graduates and students will bear these statements out, for any week of the year one of these operations is being done.

Out of the last 136 vaginal hysterectomies 56 have been performed for fibromata and 21 for ovarian menorrhagia, *i.e.*, a form of hæmorrhage associated with ovarian dysfunction in which the follicular hormone is in excess or there is absence of the corpus luteum. In 17 the operation has been connected with what I might call the pre-cancerous cervix, *i.e.*, a cervix everted, hypertrophied, eroded and lacerated up to the internal os, bleeding readily at touch and causing anæmia, menorrhagia and distress, for many days every month. You may give this type of cervix any name you wish, but pre-cancerous is what I prefer you to call it, for cancer of the cervix is astonishingly common in the tropics, and this type of cervix is the soil upon which it starts and thrives.

Three cases have been more than usually interesting in that the operations were performed for chorion epithelioma, subsequent to hydatidiform mole. One of these cases was that of a girl who had twice been curetted for hæmorrhage subsequent to the evacuation of a vesicular mole, and on each occasion the pathologist found no evidence of malignancy. Later, she came into this hospital almost exsanguine—a Zondek-Ascheim test was positive, therefore chorionic elements were present. I gave her 18 ounces of blood into the vein that

morning and did a vaginal hysterectomy the next day. She went out of hospital perfectly well and reported alive one year later. The other two cases are alive two and three years later respectively.

In five cases the operation was performed for cancer in the body of the uterus, the tubes and both ovaries being removed at the same time.

In 11 cases the Mayo operation for complete prolapse was performed. These were all old women in whom the operation could be performed in a few minutes without bleeding or shock, compared with that of the Fothergill operation.

Statistics are always dull, but I do want you to realize that the operation of vaginal hysterectomy is of peculiar importance to gynæcologists, and one of particular attractiveness to women in India. Only once have I injured the ureter and once the bladder. You need not ever be afraid of hæmorrhage or shock, or sepsis in cases of vaginal hysterectomy. There are a few points of importance which I stress to onlookers.

(1) Always double ligature the uterine artery.

(2) Always remove both the tubes for they tend to prolapse later into the vaginal wound if you do not.

(3) Always join the bases of the two broad ligaments so that they form an antero-posterior bridge across the pelvis, and thus prevent vaginal hernia later.

(4) Always use stout 21-day catgut and bring the long ends of these catgut threads through the centre of your wound to promote capillary drainage.

(5) Be sure there is no bleeding in either *cul* before closing the pelvic cavity.

(6) Always bring down the peritoneum of the base of the bladder to the edge of your vaginal incision and suture this with interrupted ligatures to the posterior vaginal incision, leaving half an inch gap in the middle line for drainage along with the catgut threads.

(7) Put in a self-retaining or soft rubber catheter for 48 hours.

(8) Fill the vagina with 1 in 100 brilliant green and then plug it tight with several strips of gauze. This is kept in for 24 hours and then removed; the patient being douched twice daily with hot saline for the next six weeks. The catgut then comes out of its own accord and the wound is healed.

(9) My patients get out of bed on the 9th day and usually leave hospital on the 12th.

The operation is really not difficult provided the pouch of Douglas and the utero-vesical pouch are quickly opened. It is the latter incision which apparently is a bugbear to the beginner, but having made the cervical incision if you boldly push up the bladder you will see the thin fish-belly-like membrane of the utero-vesical pouch. Put in an anterior retractor and

then cut this as if it were the frænum of the tongue and you are in the peritoneal cavity. From then onwards the operation is merely a matter of adroitness and anatomy.

The total mortality of my 286 cases is 0.7 per cent. I am perfectly honest when I assure you that a majority of these patients would have never submitted to any abdominal operation. Moreover you must realize that I am not in favour of radium, partly because of the expenses incurred and partly because my experience as a consultant has given me small confidence in its use.

During this period in which these 286 vaginal hysterectomies were done, with a total mortality of 4 cases, i.e., 0.7 per cent., 435 sub-total and 366 total hysterectomies have been performed with a combined mortality of 7.17 per cent. Such a mortality for abdominal hysterectomy may purchase criticism as compared with the 2 to 3 per cent. mortality of such operations in Great Britain, but it should be remembered that gynæcological surgery is only in its infancy as yet in the tropics and that India is only now entering that era which began in England with Lawson Tait and Spencer Wells.

The great majority of uterine tumours that present themselves, are in patients old, debilitated and grossly anæmic. Indeed at times it needs no little temerity to attempt any operation. With the passing of the purdah system and the growth of education, there can be no question that women will soon seek and demand surgery in the early rather than late stages of disease. It is therefore a safe prophecy that the young and bold gynæcologist has a bright future in the tropics.

Prolapse

Personal experiences are always valuable and therefore I want to say a few words about each of these five cases which I am showing you. They are all cases of prolapse of varying degrees, and my house surgeon has collected them for us because there is no gynæcological condition more common in India. Indeed there is usually a waiting list of 20 to 30 in the out-patient department.

Twenty years' experience has given one a cut-and-dried opinion on this subject and I think if a woman is young and wants more children the Fothergill operation is ideal. If she is middle aged, or desires no more children, the interposition operation, with the ligation of the tubes, is best. If, on the other hand, she is old, the prolapse is complete and there exists no pelvic diaphragm, the best results will be obtained from the Mayo-Ward operation of vaginal hysterectomy.

Very rightly you may enquire the respective merits of these operations from the point of view of the tropics. The Fothergill operation takes time—usually at least an hour—and involves the risk of shock and considerable

bleeding in patients who are already debilitated; moreover occasionally a *B. coli* infection and sloughing of the sutures occurs.

Also there is no gainsaying the fact that I have seen out here patients who have been operated upon in Manchester and other centres, in whom the uterus has remained retroverted and a source of distress. In others, subsequent to the amputation of the cervix sterility has occurred or in the event of conception dystocia has resulted, in a few, necessitating Cæsarean section. Moreover, it is not improbable that the procidentia will recur in the event of future natural delivery.

The interposition operation is very quickly performed, there is no bleeding or shock and, from the point of view of prolapse, provided a posterior colpo-perineorrhaphy is done, it is a radical cure, though perhaps like the Bassini operation for hernia it is not absolutely anatomical.

I have done a great number of these operations, both in private and in hospital, and never yet have I regretted one, though it is freely admitted that should a tumour at any future date form in the uterus removal of this organ would embrace difficulties. These patients can leave hospital in 10 to 12 days, and are astonishingly grateful, for the operation is accompanied by very little after-pain as compared with that of the Fothergill.

The Mayo-Ward operation is usually indicated in old people, and can be performed in under a half hour, which reminds me of a very useful tip that I have been making use of recently, namely, when doing any vaginal operation where bleeding may be expected, if you will inject 1 to 2 c.cm. of pituitrin into the para-cervical tissue before making your incision, there will be almost complete anæmia and hæmostasis.

The Mayo-Ward technique of vaginal hysterectomy is followed up by a posterior colpo-perineorrhaphy, but should the patient be debilitated, this part of the operation can be put off for a few weeks, and be done later under novocain.

What I want to impress upon you to-day is that pessaries have no real place in the treatment of prolapse, and that the operations are easy and should inspire no fear in the hands of a hospital surgeon. Moreover, do not forget that prolapse is a hernia and like other herniæ tends to become larger as the patient grows older and musculo-fascia gets thinner.

Abortion

In these days of economic depression it is impossible to lose sight of the fact that the conscience of the practitioner is becoming more elastic in the matter of abortion. To my mind modern laxity in the observance of the Hippocratic Oath is very regrettable, for our attitude should be a linch-pin of the State.

Unless in consultation with a *bona-fide* physician, we are assured that the health of a woman will suffer, we have no right to lend our ears to sob-stuff, lies or inventions, for remember that loose conduct on our part, although it may substantially increase a practice and enhance a reputation for kindheartedness, carries with it the boomerang of one being labelled a conscienceless petty abortionist. Every gynaecologist must perforce be somewhat of a psychologist, as he becomes involved in the problems of modern married life, with its necessity for continence or contraception. In the tropics this problem is made more acute by poverty and sickness, and the necessity of migration to England or the hills, but these considerations should not weigh with us against the balance of conscience, equity and our oath.

My own opinion is that nature must take its course provided there is no medical reasons against its doing so, but if X desires to have no more children, then with the written consent of her husband there is no reason why she should not have her tubes permanently ligated as a prophylactic measure. This is an easy operation which should be possible for any good gynaecologist to perform from below, *i.e.*, *per vaginam*.

After making a vertical incision down the anterior wall of the vagina, the bladder is pushed up, the utero-vesical peritoncum will then be seen, it is picked up by two pairs of forceps, and made to resemble the frænum of the tongue and is cut with scissors. The anterior surface of the uterus is then grasped with a cat's paw and brought downwards, the tube on one side is caught with a long forceps, pulled down, tied in two places, and cut. The other tube is similarly dealt with. The utero-vesical pouch can then be sutured, and the wound closed, or what I prefer to do is to pass two interrupted catgut sutures through one side of the vaginal flap, transfixing the anterior surface of the uterus low down and enclosing the two leaves of the cut utero-vesical pouch, the sutures emerging on the other vaginal flap. When these two ligatures are tightened, not only is the anterior pouch closed but the uterus is anteponated. The vaginal incision is then sutured with continuous catgut. The patient is allowed out of bed on the fifth day and goes home on the seventh.

This operation is very satisfactory and has no complications. It is important to be sure that the tubes are ligated and cut, and are not mistaken for the round ligament. This mistake cannot be made if the tubes, which have a mesentery and are loose with a free margin, are brought down into the incision for inspection before ligation.

Sometimes, when there is retroversion of the uterus, it is wise to vary the operative procedure by doing a vaginal shortening of the round ligaments either by performing a so-called

anterior Baldy-Webster operation or by suturing each round ligament to the anterior vaginal wall.

Obstetrics

In 1931 I published my personal results of 75 lower-uterine-segment Cæsarean sections which had been performed in the previous 4 years, and I pointed out the supreme advantage of this technique for the type of patient who in this country is seen late in difficult labour. I was able to show that in a consecutive series of such cases the foetal mortality was 13.3, and the maternal mortality—14.6. This latter figure being almost exactly half that of the maternal mortality for craniotomy or the classical Cæsarean in septic cases.

My registrar, Dr. S. C. Mukherjee, informs me that during the last 3 years there have been 5,206 confinements in the Eden Hospital. Out of these there have been 163 Cæsareans with a total maternal mortality of 9 and foetal mortality of 7. The lower-uterine-segment operation was performed on 127 patients with 5 deaths only, *i.e.*, 3.9 per cent., a gladdening figure considering the condition in which a great number of our patients arrive in hospital. In 86 of these operations, the transverse incision of the lower segment was employed. In 31 cases supra-pubic drainage was employed because an offensive liquor amnii indicated it, and in every suspiciously septic case glycerine was injected three times a day through a catheter sutured into the uterus, *i.e.*, to the cervix.

In my previous paper I pleaded for surgeons to adopt this operation in India, because there is very little hæmorrhage and practically no shock. It can be done late in labour; either late in a test labour or when the patient is seen after many examinations have been made, provided the foetal heart sounds are audible and over 100 in rate. There is practically no fear of secondary rupture of the uterine scar, because it is in a non-contractable and retractable portion of the uterus. I trust that these unbiased statistics will advance the vogue of this operation in India, especially in large teaching centres.

Before quitting the subject of Cæsarean section, I should like to make known a clinical discovery of some importance to all obstetricians, namely the extreme advantage of the fundal (McCann) incision for cases of placenta prævia. Our mortality from hæmorrhage before I discovered this was very high, but during the last three years no mother has been lost. This area of the uterus, where fusion of the Mullerian ducts occurs, is practically bloodless and if the assistant firmly controls the lower pole of the uterus in his grasp there is practically no bleeding while the surgeon, with his finger between the uterine wall and the membranes, removes the foetal sack with the placenta intact.

Puerperal Sepsis

Again and again during the last year I have been drumming into my students the advantages of the Hobbs' glycerine treatment, and have pointed out how this technique, not only lessens the grave risks of puerperal sepsis in the tropics, but diminishes the stay of patients in hospital by almost exactly half the number of days—a matter of great importance from an administrative point of view in these times of financial distress.

In order to convince you, my registrar has furnished me with the following data which speak for themselves.

In the five years, 1922–1926, before we adopted the Hobbs' treatment, there were 5,796 confinements. The incidence of puerperal sepsis per mille was 100.95 and there were 46 deaths, i.e., 7.8 per mille.

From 1927 to 1931, when Hobbs' treatment was only occasionally employed, there were 7,061 confinements. The incidence of puerperal sepsis was 122.53 per mille and there were 45 deaths, i.e., 6.5 per mille.

During the whole year of 1932 in which I have been using the glycerine treatment intensively, by this I mean that on the first suspicion of sepsis a catheter is sutured into the uterus, for the injection of glycerine three times a day; there have been 1,940 confinements. The incidence of puerperal sepsis was 109.28 per mille and there were 3 deaths, i.e., 1.54 per mille only.

Moreover during the last 12 months I have entirely given up the use of antistreptococcal serum and substituted injections of Aolan, or skimmed milk. In addition no student, doctor or nurse was allowed to be in attendance on any labour case without a properly-adjusted mask over the nose and mouth. Brilliant green 1 in 100 was the only antiseptic used.

From a tropical point of view it may be that all these factors have combined to give us a record year as regards the paucity of deaths from puerperal sepsis, but my own impression is that the main credit is due to the keen work of my staff and the efficiency of the glycerine treatment, for all of you know the dreadful condition in which large numbers of our patients are brought into hospital after hours in labour and much mishandling.

The moral these statistics clearly demonstrate is one of enormous importance to every doctor and to every woman's hospital in the tropics—namely, that they have in the glycerine treatment and the injection of milk, together with the use of brilliant green and masks, a sure method of combating one of the greatest perils attaching to obstetrics.

My house staff will be very pleased to show any of you with what ease and simplicity a catheter can be inserted and sutured to the cervix of a puerperal patient without pain or fuss.

Most earnestly I beg you to accept the lesson of this method and these statistics.

YAWS IN THE NICOBAR ISLANDS*

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INCIDENCE of yaws in the Nicobar islands is not mentioned in standard books on tropical medicine. I have received reports from time to time, since my arrival in Port Blair, that syphilis is very prevalent in the Nicobars, causing severe disfiguration of the inhabitants and threatening the extinction of the race. Two typical cases of yaws in the secondary stage were noticed by me among Nicobarese, who were sent to Port Blair in 1930 for a trial for murder, these were cured with two injections of novarsenobillon (0.6 and 0.9 grammes). This led me to suspect that the cases reported to be suffering from syphilis in the Nicobars might be cases of yaws. I understand that Lieut.-Col. Barker, I.M.S. (1925) reported a case of yaws from the Nicobars, but I fail to find any other record of the prevalence of this disease in the Nicobars. An opportunity occurred for investigation when the census superintendent for the Andaman and Nicobar islands required the services of a sub-assistant surgeon to record anthropological measurements of the Andamanese and Nicobarese in connection with the census report for these islands. Dr. Naidu was deputed for this work and I sent him well equipped with, I considered, an adequate supply of novarsenobillon in the hope of temporarily ameliorating the condition of the people, and awaited a report from him as to any further steps to be taken to combat the disease. I may mention that the Andaman islands are free from yaws, while syphilis and gonorrhoea are common and are principally responsible for undermining the fertility of the aborigines. Dr. Naidu worked under difficult conditions with regard to language, the time limit, and discomfort of a camp life, from 7th February, 1931, to 18th March, 1931. From his report, it would appear that an interesting study of tropical diseases could be made in these islands. The principal diseases prevalent in both the great and little Nicobars are yaws and elephantiasis. Altogether he treated 60 cases of yaws.

He also noticed that at Chowra, out of a total population of about 600, 35 were showing visible signs of elephantiasis. During the course of his whole journey he came across only two cases of syphilis—one contracted at Nancowry and the other at Car Nicobar—both trading centres for the outside world with a floating population of eastern nationals. He had a large out-patients' attendance wherever he camped.

* A résumé of a lecture delivered at the Clinical Society of Port Blair on 13th February, 1932.

The people from different islands appreciated the treatment given and expressed a desire to Mr. Bonington, census superintendent, and to Dr. Naidu that they wanted the whole-time services of a doctor for the island. If a doctor would be appointed for them, Teressa or Comorta would be a suitable central place for a hospital or dispensary. As regards medical facilities for the Nicobars, a doctor, appointed by the Car Nicobar Mission (subsidised by local Government), is stationed at Car Nicobar in charge of a hospital, and a small dispensary in charge of a compounder is established at Nancowry, but there are no amenities for treatment at any of the other islands, and only in fine weather can the inhabitants go to these two centres. Dr. Naidu exhausted his stock of novarsenobillon in treating cases of yaws before he returned. On receiving his report I proceeded to the Nicobars with Dr. Naidu, in April 1931, with a plentiful supply of novarsenobillon. We took the opportunity of examining some of the cases that had received an injection two months previously. The inhabitants were so impressed with the efficacy of the treatment that more cases eagerly sought treatment and another 47 cases were treated.

This number would have been considerably bigger if it had been possible to send information of our impending visit to the various villages. The cases that had received an injection in February or March had all healed up with the exception of two who still manifested latent infection and indolent sores. These were given a second injection.

Yaws (Frambæsia)

Local synonyms for yaws, 'Aiyoke' (Teressa) and 'Aiyak' (Chowra), and for syphilis 'Thannoi' and 'Sakayace'. Although they do not bear any relation to the native names mentioned by Manson or Castellani, there is a resemblance in phonation in the local synonyms in the two islands, while it is noteworthy that the names for syphilis are distinct and definite without any such similarity.

Geographical distribution

The Nicobar islands may be regarded as a continuation of the chains of islands of the Malay archipelago and are adjacent to other endemic area of yaws; viz, Upper Burma, Assam, Siam, Ceylon, Java, and Sumatra.

While it has been observed by authorities on yaws that the disease has a predilection for certain native races, particularly of the negro or negrito stock, it is not known among the Andamanese who belong to the negrito stock, although syphilis is very common among them, and yaws exists endemically within 150 miles of these islands.

Epidemiology

The sanitation is primitive and conditions are ideal for the maintenance of infection. The

people live in primitive huts whose floors and walls may be impregnated with infection. Where human beings, dogs and pigs live huddled together, it is easy to understand how this disease spreads rapidly.

It is quite possible that house infection is important, judging by the habits of the people, but from the innumerable flies we saw settling on yaws sores it is easily conceivable how these convey the spirochaetes to pre-existing breaches of skin of the inhabitants.

The principal occupations of the people are cultivation of cocoanut and tobacco, pig herding, and fishing.

Ætiology

In our series adults were most commonly affected. We could not get information regarding their age, but, guessing from their appearance, it is most common amongst men between 20 and 30 years and amongst women about 25. The youngest patient was 3 years old, and the oldest 45. In our series there were 26 men, 8 women and 4 boys.

As regards the local theory of the causation of the disease, people of Chowra were not able to offer any suggestion, while in Teressa they attributed it to eating papaya fruit; they believe that this is heating to the body, and that the rash thus brought out is aggravated by the itching produced by the bites of mosquitoes and flies.

Causative organisms.—Conditions did not favour extensive laboratory examinations, but we were unable to demonstrate the spirochæte in scrapings from the sores. Wassermann reactions were not done and the diagnosis of cases is entirely based on clinical and therapeutical evidence. We did not come across any case where yaws and syphilis coexisted. Only two cases of secondary syphilis with typical eruptions were seen by us and the eruptions were so distinct from those of secondary yaws that one could not mistake them clinically. As the disease was seen mostly in young adults, no case of endarteritis or arterio-sclerosis was noticed; this however is very rare in yaws, although common in syphilis, and is useful in the differential diagnosis of the two diseases.

Incubation period

No definite information could be obtained from the people at Teressa or Chowra regarding the incubation period. Some of the Chowra people thought that it might be one month. The period is probably a longer one. The source of infection in one patient was traced more or less definitely. A case of yaws from Chowra went to stay with her friends at Nancowry and a woman in whose house she was staying developed yaws three months after the former had left her house and returned to Chowra. No other history of exposure to infection could be traced, so that a period of 92 days given as the maximum in some of the

books appears to correspond in this case. We have of course to take into consideration that their idea of dates is somewhat different from ours.

Primary stage

'Madre Buba or Mother Yaws'. An infiltrated papule develops at the site of inoculation or a granuloma in an old skin lesion, such as an ulcer, an itch pustule, an insect bite, or any abrasion or scratch incidental to a jungle life. In the initial stage, they complained of intense itching, lasting for about a week. It is interesting to compare this with the chronic infective granulomatous condition common on the neck and hump in cattle in Port Blair. In our series, the lower part of the leg was the site of predilection, other common sites being the thighs, arms, buttocks, and groins—all extragenital. No case was seen of primary lesion on the breasts of nursing mothers or mouths of suckling babies, nor in women at the bend of the elbow nor on the hip. The lesion is remarkably persistent lasting even up to a year, or it may heal up in about a week to 2 months time, leaving a white scar (no pigment). If the sore does not heal, it begins to enlarge and in about a week's time from its appearance it begins to ooze a yellowish secretion, with the itching consequent to intense local irritation, or it becomes covered with a thick crust or scab, due to inspissation of the secretion. Constitutional symptoms were negligible in the patients examined and interrogated by us, and the lesions did not incapacitate them from work for any appreciable period. Pain was complained of by patients both at Chowra and Teressa particularly in the early stages, but it disappeared when the yaws was fully matured. Although induration is said not to be the rule, this was noticed in half the cases. Enlargement of the lymphatic glands was not conspicuous and there was not a single case of suppurative glands in any of the three stages.

This stage lasts from few weeks to several months, in our series the average duration was 3 months and the primary lesion was present in most cases with secondary eruptions.

No treatment was adopted by them in the early stage and it was not until the yaws became a large granulating ulcer that treatment by application of leaves was resorted to.

Secondary stage, or stage of generalised eruptions

The onset of this stage corresponds with the decline of constitutional symptoms and most of our cases treated were well advanced in the secondary stage. Generalised eruption is ushered in as follows:—Minute roundish papules of the size of a pin-head are seen, with a yellow crust at the apex, usually three months after the primary lesion, lasting a few weeks and leaving, when they disappear, furfuraceous patches; these patches are circular and show a

fine sand-coloured desquamation as if the skin has been dusted over with flour or *atta*. This condition was only noticed in one of our cases. Some papules coalesce, enlarge, and the skin gets proliferated or hyperkeratoid.

'Keratoid exanthem' of Scobe and Sellard, which is common on the face and limbs persisting throughout the attack of yaws, was not seen in our cases, nor was pigmentation present in any of them. The eruption is very characteristic; from its appearance resembling a raspberry it is called 'frambœsia'. Papules appear around the primary sore. The itching produced by these is intense. Like syphilis, the eruption is pleomorphic, scaly, papular, roscolar or ulcerative, and appears on exposed situations and on the anterior surfaces. The common sites are the legs, forearms, arms, thighs, groins, trunk and face; only one case of scrotal infection was seen. There is no pain and the peculiar offensive sour or musty odour, due to infection with Vincent's bacilli, was absent in our series. Papules appear in regular constellations, large ones being surrounded by satellites. Auto-inoculation is probably responsible for their symmetrical appearance on contiguous areas of skin or mucous membranes, such as the anus, groin, angles of mouth, and vulva. Other characteristics in our series which correspond with the general description in books are that the eruption is painless, mucous membranes and bones are unaffected, there were no eye symptoms, and the patient was able to attend to his work throughout this stage.

No case of 'ringworm' yaws was seen. Not a single case of hyperpigmentation was noticed by us. Only one case of arthritis of the knee was seen, although arthritis of both large and small joints is said to be common.

Periostitis was common, particularly in the digital phalanges. There were no nervous symptoms; hyperhidrosis, a sign confined to hand and soles particularly in children, was not seen.

Tertiary stage

This is a stage of gummatous nodules and deep ulcerative processes. The transition period between secondary and tertiary stages differs widely from that of syphilis. Instead of getting absorbed and healing, yaws may spread marginally, as well as deeply, and lead to extensive ulcers which may last for years. Such ulcers may involve deep structures, producing necrosis of bone or cartilage, or give rise to cicatricial contractures.

Onychia, paronychia, atrophy, and shading of nails were present in a few cases. Multiple dactylitis with uniform swelling of the phalanges was noticed in the case where the tibia, forearm and clavicle were also affected by periostitis.

Yaws on the soles of feet is limited by thick skin. Like an abscess in this region, it is

under high tension. It attains a large size before it bursts and is therefore very painful. When the thick epidermis gives way, this is converted into a fungating ulcer and, although painful to the touch, is not painful to the same degree as it was before it burst through the skin. This ulcer, after the pent-up secretion oozes out, appears like the section of a pomegranate cut through with a knife. In one of our cases this condition had lasted over two years and showed no signs of healing even along the margins, which were thick and indurated. Perhaps want of dressing, and constant irritation from dirt are responsible for the prolonged duration in this case. The lesions were unilateral.

One case of 'clavus' was also seen.

'Gangosa'

This is a destructive, disfiguring process with deep ulceration of the nose and pharynx, and is said to commence as an ulcer of the soft palate. It spreads slowly and leads to complete destruction of the hard palate, the soft parts, cartilage and bones of the nose, in some cases sparing the upper lip which forms a bridge, in other cases leading to its partial destruction. A great cavity is left with the tongue, which remains unaffected, as the floor. Two typical cases of this condition were seen. A third case showed spontaneous arrest—duration about six years. The larynx was unaffected, articulation was seriously impaired, but phonation was retained. There were no other bone lesions in these cases. The age of the three patients was between 35 and 45.

Bone lesions

These are common in the tertiary stage. As in syphilis there are painful nodes on the anterior surfaces of long bones, such as the tibia, radius, ulna and clavicle, which are hard, tender, and painful in the beginning, and remain as thickenings when the acuteness subsides.

The characteristic sabre-shaped deformity of the long bones affecting the tibia, forearms, arms, and clavicle was noticed in one case.

Fibrotic tumours, called juxta-articular nodules, over the olecranon and lower end of the femur, which are painless and multiple were seen only in one case.

Skin lesions

Healing of subcutaneous gummata with loss of pigmentation of skin resulting in leucodermic patches is common and unlike syphilis it is not confined to the hands, ankles, wrists, feet and palms.

General health

In spite of the animistic ideas of the inhabitants, they appear to be grateful for western

methods of treatment and they need no persuasion to be injected, as after the first course of injections given they gain faith as to the efficiency of our method of curing the disease.

They believe that it is a chronic disease, but not a fatal disease. Although at Teressa, many adults are reported to have died of the disease, at Chowra only 3 children under 10 have died from yaws within the last 3 years. We have to take into consideration an outbreak of small-pox which may have been responsible for the large number of deaths reported at Teressa.

Relapses are not common and one attack confers immunity. It has been observed by investigators that 'apparently saturation of a community with yaws virus produces a relative immunity to syphilis' and this may account for the few cases of syphilis seen on these islands.

Treatment

With the limited time at our disposal the only treatment tried was injections of novarsenobillon,

0.9 gramme for adults,

0.6 gramme for young adults,

0.3 gramme for children up to 10 years of age.

One injection appears to have cured most of the cases, although this needs confirmation by a second visit to the islands to examine the cases that have been injected.

Treatment adopted by the Nicobarese

At Chowra, application of certain leaves, *Rafab*, according to them appear to check the disease. At Teressa, the ulcers are rubbed with sand and then washed in sea water; this is supposed to irritate the ulcers and assist cleaning; a paste of leaves (*Ramintho*), made by boiling and grinding, is then applied. Ulcers are said to disappear in a few cases after a series of applications. The inhabitants appear healthy and well nourished, and yaws did not affect their general health, so that the prescription of tonics and good food as general treatment was not necessary in them.

Prophylaxis

It is evident that direct contact is the usual method of transmission of the disease from person to person. According to Manson-Bahr, blood-sucking insects may be responsible, but, in the Nicobars, flies appear to us to be the more likely agents. The local theory of communicability in certain islands is that partaking of contaminated food produces yaws. In my opinion the only way of adopting prophylactic measures for the eradication of the disease is to appoint a medical officer with a steam launch at his disposal for one year, so that he can visit all the islands in turn periodically and give

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THE RÔLE OF CHÆTOPODS (SEGMENTED WORMS) IN THEIR RELATION TO MAN

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(Read before the Indian Science Congress, 1933)

THE Annelid worms comprised within the orders of the Oligochætes (earth-worms) and Polychætes (sea-worms) do not often come within the purview of the medical man or pathologist, although the occasions on which they do so are interesting and sometimes important. It is from the economic point of view that they must be assessed to be of much greater interest to man.

Their economic importance was pointed out of course by Charles Darwin who realised what a vast influence the earth-worms have in the cosmogony of Nature by their uplifting of the soil and amplifying the bounties of plant life to man. Then the aquatic species provide fish with much of their food, for example the Oligochæte Tubifex, which burrows in the soft mud of shallow collections of water, is preyed upon by fish just as are the earth-worms on land by birds, and likewise the Polychætes, or bristle-worms, which live in the sand or slime on the bed of the sea or tidal rivers, provide food for vast numbers of fish, these worms indeed being sometimes used as baits by fishermen. And more directly than this, man sometimes uses these creatures for food; Professor Percy Moore of Pennsylvania University has informed us that he has seen Italians engaged on rail-construction in the United States using earth-worms for making soup, the worms being boiled and the solids then strained off and discarded. They cannot however be considered to have much direct food value to man, otherwise they would not exist in such numbers as they do while poor beggars are rummaging in dustbins for scraps of food. At any rate we are told by Dr. Hutton on the authority of a friend of

(Continued from previous page)

appropriate treatment where necessary. Each endemic area needs to be visited at least once in three months.

In conclusion, I wish to express my thanks to Dr. D. Naidu for his loyal co-operation and help in collecting statistics and local information, and in treating cases under adverse conditions.

REFERENCE

Barker, F. A. (1925). A Case of Frambœsia in the Nicobar Islands. *Indian Med. Gaz.*, Vol. LX, p. 29.

his who made a 'practice of experimenting on every sort of animal and insect food' that they are 'uninteresting' to the palate.

While the Chætopods have not yet made their appearance in the pharmacopœias of any 'western system' of medicine one may note that they are made use of in certain other 'systems', and in this connection we cite Gate (1925):—

'Worms are used in various preparations by the native doctors both in Burma and India. In Burma the most important use is in treatment of a disease called "Ye se kun byo", the symptoms of which as described by Burmans greatly suggest pyorrhœa. The worms are prepared by heating in a closed pot until reduced to ashes. The ashes are either used alone as a tooth-powder, or to the ashes are added roasted and pounded tamarind seeds, and unseasoned betel-nuts to make up the powder. This is supposed to be a sure cure for the disease. When attempts have been made to learn which species of worms are used for this medicine, the answer is invariably, "Oh, just the common one found crawling around during the rain".

In a disease called "Mc kha yu" the symptoms of which are white-spots on the tongue and membrane of the mouth, slight fever, laxity of the bowel, and, in very small children, inability to suckle, the remedy is worm-ash applied to the spots in the mouth. It is also used similarly for canker.

A disease called "Kalay yawga", the symptoms of which are vomiting, laxness of bowels, and excessive thirst. For this earth-worm castings are roasted, shaken thoroughly in water, and the clear fluid decanted. Dose—a cupful to be drunk once a day. This is said to be "very cool medicine for hot stomach".

A disease called "Mainma mecphwa noyeekhun thwaykhan". Symptoms are general weakness after pregnancy and inability to nurse the child. The common worms are boiled in water with salt and onions. The clear fluid is decanted and mixed with curry or other food.

A disease called "Panthay ana", the symptoms suggesting impotency. The oil from the bodies of three toadstools is mixed with five ticals weight of sesamum oil. In the mixture three large worms are boiled. The oil is decanted and used to massage the penis. This is said to be "exceedingly powerful medicine".

The earthworm *Lumbricus* is used by quacks in India and in some cases by the Kavirajes as a medicine. It is boiled in pure mustard oil and the preparation applied as an antiseptic to ulcers and sinuses.

The body-juice of fresh *Lumbricus* mixed with fresh raw milk or butter is often widely used for aphthous and ulcerative stomatitis not yielding to other medicines.

Such are the examples of Chætopods in their rôle of utility to man. From the medical standpoint we have a few but interesting records.

From the public health side we have found earth-worms in their early stages appearing in the water-supply of large cities. In one case that came to our notice it was thought that the young worms had migrated through the soil down to the mains and been sucked in to the pipes through a gap in the joints.

On the other hand we have a few reports of Oligochætes 'parasitising' man.

Curling (1839), cited by Blanchard (Blanchard and Savignac, 1910) reported 'worms'

Dactylus aculeatus from the urine of a child. They were thought to be helminths, but the figures given suggested that they were the Oligochaete species *Euchytraeus albidus* Henle.

Waldenstrom in 1873, cited by Blanchard (Blanchard and Savignac, 1910), reported a case in which there was a vaginal discharge, irritation of the pudenda, and the patient complained of violent pains on any movement. After about a year a common earth-worm emerged from the vulva and the pain ceased immediately. Apparently the worm had caused the symptoms; the pain was probably due to the setae, and the creature had lived for such a long period as a 'pseudo-parasite'.

Bergh in 1885, cited by Blanchard (Blanchard and Savignac, 1910), *q.v.*, found *Euchytraeus buchholzi* in the mouth of a patient suffering from weakness, salivation, and vertigo. Possibly this species had been imbibed with well-water. The author thought that after entering the stomach it had later been evacuated into the mouth.

Hanau in 1899, cited also by Blanchard (Blanchard and Savignac, 1910), reported the case of a young woman who affirmed that certain worms which she exhibited had come from a perityphlic fistula of 4 years' standing. They were identified as *Henlea nasuta* and *Microcolex modestus*. But she later confessed to having placed earth around the opening of the fistula 'in order to keep it fresh'.

Delage in 1905, cited again by Blanchard (Blanchard and Savignac, 1910), recovered a specimen of *Allolobophora fætida* from the urine of a patient.

Blanchard and Savignac (1910) gave a detailed account of a case watched for over 4 years in which there was reported nausea and general malaise, simple or bilious vomiting, and indigestion, and in which some worms were discovered by the patient in the vomit. These worms were *Henlea nasuta* and *Friederica bisetosa*, they were always produced dead, and none appeared in the stools. The authors finally concluded that the case was one of neuromimesis.

Heymons (1926), described the passing of *Pachydrius lineatus* on two occasions in one week. He was inclined to disregard the occurrence as accidental until two others came to his notice, leading him to the opinion that the species being very adaptable in its habits might very well come to live in the human intestine.

Müller (1927), later asserted that there was no doubt about this worm's ability to live in the human intestine as he was aware of a case of abdominal trouble which had been relieved when a number of the worms had been passed.

With regard to the Polychæta in relation to pathology we have the following records:—

Biswas and Strickland (1927) described a living polychæte worm of the genus *Nereis*, a mature, active individual about an inch long, which was discharged in muco-pus from the nose of a patient after much coughing and sneezing in the course of an acute and painful attack of coryza due to, or aggravated by, the presence of the worm. Although Nereids are typical marine worms, some of them, like a great diversity of other marine animals, have considerable power of adaptation to the sundry tidal and seasonal variations of deltaic waters, such as the Hooghly at Calcutta. What is remarkable is that the creature should have found its way unnoticed into a man's nasopharynx, and having done so, could have lived there for a week or more.

Dr. Sur, of the Calcutta Medical College, has brought to our notice another worm, which has been kindly identified for us by Mr. Monro of the British Museum as *Nereis (Lycoris) verrilli*, Grube. The specimen was a typical Indian marine species and showed no signs of having been affected by intestinal juices. It lived for about 3 days in tap water and then another 4 days in normal saline, in which it laid a large number of eggs which did not hatch out. It was passed in the stool by an apparently-healthy child about 2 years old. It was detected moving in the child's motion when the mother went to wash it away from the floor of the house where it had been evacuated.

Conclusion

We may conclude by asserting the vastly greater importance of these worms to man from the economic point of view rather than the medical. The comparatively few medical cases that have been reported may be grouped into two classes, firstly those of interest to the psychiatrist, and secondly those to the surgeon or gynæcologist, these being probably all due to contamination of the water in the use of man, the worms adapting themselves to such diverse situations as the vagina, nasopharynx and intestine.

REFERENCES

- Biswas, L. M., and Strickland, C. (1927). A Strange Parasite of Man. *Indian Med. Gaz.*, Vol. LXII, p. 256.
 Blanchard, R., and Savignac, R. (1910). Pseudo-parasitisme des Oligochètes chez l'homme. *Arch. Parasit.*, Vol. XIV, p. 40.
 Curling (1839). Annelids in Man. *Med. Chir. Trans.*, Vol. IV, p. 274.
 Gates, G. E. (1925). Earth Worms. *Journ. Burma Res. Soc.*, Vol. XV, Part III, p. 196.
 Hanau, A. (1899). Wahrscheinlicher Pseudo-parasitismus von Schmeissfliegenlarven, etc. *Arch. Parasit.*, Vol. II, p. 23.
 Heymons, R. (1926). Ein Borstenwurm als angeblicher Insasse des menschlichen körpers. *Centralbl. Bakt.*, Vol. XCIX, p. 153.
 Müller, R. (1927). Borstenwürmer in menschlichen Körper. *Centralbl. Bakt.*, CI, p. 151.

Indian Medical Gazette

MARCH

SIXTH BRITISH PHARMACOPŒIA (1932)*

MANY years ago it was laid down that the object of a pharmacopœia was to select from among substances which have medicinal power those whose utility is most fully established and best understood, and to form from them preparations in which their powers may be exerted to the greatest advantage. The modern pharmacopœia has, however, become more a book of standards, its fundamental object being to provide standards for drugs and medicines of therapeutic usefulness which have a wide application in medical practice. It lays down tests for the identity, quality, and purity of drugs. That there should be such a standard for drugs intended for the use of physicians is imperative in order to ensure uniformity in their activity and physical properties, to make certain that an article sold under a pharmacopœial name conforms to the pharmacopœial standards, and to provide a basis for the legal control of pharmacopœial substances. It should be realised, however, that in Great Britain the British Pharmacopœia is accepted only as a 'presumptive standard', and is not recognised by legislation, as it is in some of the Dominions. The pharmacopœia is, moreover, the chief safeguard of one of the most time-honoured principles of the medical profession, namely that there must be no secrets about the drugs used in the treatment of disease. The physician must have full knowledge of all the constituents and of all the properties of the drugs he prescribes; there can be no compromise. The physician should always bear in mind that he is the sole judge of what is suitable for his patient.

As a national pharmacopœia is primarily meant to meet the claims and satisfy the needs of physicians of its own particular country and period, there must exist differences not only between pharmacopœias of various countries, but also between various editions of the same pharmacopœia. In almost all countries, therefore, the national pharmacopœias are produced by a recognised authority, and in many directly under the supervision of the State; the noteworthy exceptions to this latter practice are the United States of America and Great Britain.

Attempts have been made to form an international pharmacopœia; in 1925 the second international conference on the unification of the formulæ of powerful medicaments held its sitting in Brussels and drew up a scheme for an international agreement. This agreement was completed in 1930 with the concurrence of the British Government, who, however, rightly reserved the right of introducing modifications in detail in accordance with established usage or the progress of medical and pharmaceutical science. The desirability of maintaining standards on an international basis for powerful and dangerous drugs, especially narcotics, is obvious, but so also are the difficulties in the way of complete internationalization of pharmacopœias. What has been achieved so far on these lines is satisfactory, but we can see great disadvantages in pursuing unification too far, and we consider that each country should evolve a pharmacopœia best suited to its own peculiar climatic and racial factors, with due regard to the raw material available within the country, and without departing from the international standards.

The British Pharmacopœia is produced under the authority of the General Medical Council by the Medical Acts of 1858 and 1862, and the first edition of this work appeared in 1864. Subsequently, several editions have appeared at irregular intervals; the fifth pharmacopœia was published in 1914 and the most recent, the sixth, made its appearance late in 1932, the first copies arriving in India a few months ago. Very considerable credit is due to the pharmacopœia commission, a body of eight distinguished members of the medical and pharmaceutical professions in Great Britain, who after three and a half years of intensive labour produced the new British Pharmacopœia, which in the opinion of many eminent authorities is the most systematic and efficient that has so far appeared. The actual work of preparing various sections was delegated to sub-committees of experts in various branches and they in their turn were advised by pharmacopœia committees in different parts of the British Empire; at the same time close contact was maintained with the corresponding American authority responsible for the revision of the United States Pharmacopœia, which is now already proceeding with its labours for a revised edition due in 1935. In order to keep pace with modern developments the commission has proposed that new editions should henceforth be published regularly at ten years intervals; and it is hoped that in future the British and United States Pharmacopœias will alternate about every five years.

The appearance of this new pharmacopœia is an event of considerable importance, not only to the medical profession but to the profession of pharmacy, as the training and examination of pharmacists are based upon it, and their daily practice is influenced by it.

* *The British Pharmacopœia*, 1932. Published under the direction of the General Council of Medical Education and Registration of the United Kingdom, for the General Medical Council, by Constable & Co., London, 1932. Pp. xlix plus 713. Price 21s. Obtainable from the Oxford University Press and all booksellers.

In preparing the present pharmacopœia the commission has worked on the principle that only those standard articles should be included which are in use throughout the British Empire. Those drugs or substitutes which have a purely local use have been left out with the idea that they will be defined in supplements or *addenda* prepared by the authorities of the countries concerned. It thus comes about that although there are a large number of additions, which was to be expected, there are also an even larger number of omissions. Nevertheless, the book is larger than the 1914 edition; there are 641 pages, excluding the index. More details are given in the monographs than in the previous editions and new tests are introduced. The appendices cover about 150 pages and include various analytical data, and methods for the biological assay of drugs.

In the last pharmacopœia there were numerous instances in which a group of drugs had almost identical therapeutic action; in the new pharmacopœia only one member of the group has been selected for inclusion. The *hypodermic injections* have been omitted altogether, as it is considered preferable that the practitioner should prescribe the dose of the active material, as such. In deference to the 'International Agreement', the *vina* have been excluded, and simple solutions of chemical substances will no longer masquerade under the name *tincture*, e.g., *tincture* of iodine is now *solution* of iodine. The infusions are now known as *fresh infusions*, and *concentrated infusions* have been introduced; the concentrated infusion of *digitalis* is not 'official'. *Oculenta*, ointments for the eye, have been introduced, but amongst the *unguenta* there have been many deletions. Other important additions are toxins and antitoxins, vaccines, sera, gases (oxygen, carbon dioxide, ethylene, nitrous oxide), a vitamin-D preparation, liquor *ergosteralis irradiati*, standardised powdered thyroid, and a host of new and approved chemicals and derivatives. Altogether, one hundred and thirty substances appear for the first time in this edition. On the other hand, sixty-one crude drugs, sixty-eight chemicals, and two hundred and twenty-eight galenicals that appeared in the 1914 edition have been entirely eliminated. The omissions include quite a number of Indian and colonial drugs and preparations, and we feel that the profession in India will note with regret the disappearance of a large number of drugs of Indian origin which were included either in the 1914 edition or in the Indian and colonial *addendum* to the British Pharmacopœia of 1898. A list of the principal omissions in this connection is given below.

Acaciæ cortex, *aconitina* and *tinctura aconitinæ*, *anisi fructus* and *aqua anisi*, *aqua aurantii floris*, *aqua carui*, *aqua fœniculi*, *aqua rosæ* and rose petals, *aurantii cortex indicus*, *belæ fructus*, *extractum belæ liquidum*, *berberis* and *tinctura berberidis*, *betel*, *buteæ gummi* and *buteæ semina*, *cannabis indica*, *tinctura cannabis indicæ* and

extractum cannabis indicæ, *cassiæ fructus*, *catechu nigrum*, *trochiscus catechu* and *pulvis catechu compositum*, *chirata* and *tinctura chiratæ* and *infusum chiratæ*, *cubebæ fructus*, *cucurbita semina preparata*, *tinctura cantharidii*, *cusso*, *daturæ folia* and *tinctura daturæ seminum*, *ispaghula* and *decoctum ispaghulæ*, *embelia*, *gummi indicum*, *jalapæ resina*, *kaladana*, *kaladanæ resina*, *pulvis kaladanæ compositum*, *myrobalanum*, *unguentum myrobalani*, *unguentum myrobalani cum opio*, *oleum ajowan*, *oleum chaulmoogræ*, *picrorhiza*, *pyrethri radix* and *tinctura pyrethri*, *tinctura podophylli* and *podophylli indica*, *syrupus urginæ*, *valerianæ indicæ rhizoma*, and *viburnum*.

Although the majority of the drugs referred to in this list are not universally used in the Empire and are not generally efficacious enough to merit inclusion in the new Pharmacopœia, some of them, such as *cannabis indica*, *datura*, *belæ fructus*, *chirata*, and *kaladana* are bound to be missed by the profession. These drugs are known to be potent and are used not only in India but in the colonies also. Besides these, *berberis* has recently been shown to be extremely useful in the treatment of the oriental sore and an ointment made from it is extensively used in trachoma and certain skin conditions. *Picrorhiza kurroa* contains practically the same active principles as the *Gentian kurro* of the pharmacopœia and can be effectively substituted for the official gentian. *Plantago ovata* (*ispaghula*) seeds have recently become a favourite laxative in the West. In America and France, the seeds are in great demand, and have been claimed to possess therapeutic properties in no way inferior to liquid paraffin preparations, so commonly used in habitual constipation. In India the seeds have been in use for many centuries in the treatment of dysentery and diarrhœa. Apart from these, there are a number of drugs used in the indigenous medicine which have been found effective after careful trials by many authorities. To this category belong *Holarrhena antidysenterica* (*kurchi*) for dysentery, *Taraktogenos kurzii* (*chaulmoogra*) for leprosy, *Saussurea lappa* (*kuth*) for asthma, *Bærrhaavia diffusa* (*punar-nava*) for dropsy, and many others which are extensively used by practitioners. Some of these drugs are of interest to India only, others are universally used. Now that these are no longer recognised as 'official' in the British Pharmacopœia, recognition in some other form appears to us to be essential. The question of the advisability of compiling an Indian Pharmacopœia was considered by the Drugs Enquiry Committee, whose report was issued last year. The evidence before this committee left no room for doubt that India should have an official publication which would record what she recognises as a trustworthy and approved *materia medica* of her own. It was the opinion of that committee that an Indian Pharmacopœia should be prepared on the lines of the British and United States Pharmacopœias; this pharmacopœia should include only drugs of known composition, of definite pharmacological action, and of well-established therapeutic use,

whose toxicity has been fully investigated, and for which the necessary standards for determining a safe maximum dose have been worked out by chemical or biological methods. The work that will have to be done before such a pharmacopœia can be completed will take a considerable amount of time, as the field for investigation is a very wide one and up to the present only a very small percentage of the drugs used in this country have been properly standardised as to their composition and therapeutic activity. In the absence of any scientific information regarding the majority of drugs used in the indigenous systems of medicine and in view of the fact that important pharmacopœial drugs of general interest to the Empire, and growing in India, have not been fully dealt with in the 1932 edition of the Pharmacopœia, our present most pressing need is the preparation of a good Indian *addendum* or supplement in which all the available information concerning the important drugs of Indian origin can be obtained.

On p. 51 of our January issue we reviewed a book on the indigenous drugs of India* written by Lieut.-Colonel R. N. Chopra, I.M.S., who was the chairman of the Drugs Enquiry Committee, referred to above. In this book has been gathered all the information available on the

* *Indigenous Drugs of India*. By Lieut.-Col. R. N. Chopra, M.A., M.D. (Cantab.), I.M.S. Calcutta: The Art Press, 1933. Pp. xxii plus 655. Price, Rs. 15. Obtainable from Thacker's Medical Book Dept., Box No. 54, Calcutta, and all booksellers.

subject of drugs of Indian origin used in the western pharmacopœias and of drugs of all kinds used in the Indian indigenous systems. Amongst the latter there are a number the medicinal value of which has been scientifically established, and there are probably many more which when investigated will be put in this category; included amongst the former are those drugs that we have detailed above as being in the old pharmacopœia, or in the colonial and Indian *addendum*, but excluded from the new pharmacopœia. The information given about these drugs is very complete, and is even more detailed than would be required in a pharmacopœia. This book will constitute a valuable supplement to the British Pharmacopœia for physicians and pharmaceutical chemists practising in India, until such time as the Indian *addendum* to the present pharmacopœia has been prepared, and there is little doubt that when this *addendum* is prepared this book will form a sound basis on which to work.

In conclusion, we will summarize our remarks by saying that the new British Pharmacopœia is in every way a most satisfactory production. We offer no criticism for the policy of excluding a large number of Indian-grown drugs which are mainly used in India, as the intention of the compilers was obvious, namely that India should prepare her own pharmacopœia, or *addendum*. It has now become more essential than ever that as little time as possible should be lost in putting into effect the recommendation of the Drugs Enquiry Committee in this particular connection.

Medical News

TWENTIETH INDIAN SCIENCE CONGRESS, PATNA, 1933

SECTION OF MEDICAL AND VETERINARY RESEARCH

President:—A. D. STEWART, M.B., F.R.C.S.E.,
D.P.H., D.T.M. & H.

LIEUTENANT-COLONEL, I.M.S.

Presidential Address

SOME REFLECTIONS ON MEDICAL SCIENCE AND PUBLIC HEALTH

GENTLEMEN,

Your choice of President of the Medical and Veterinary Section of the Indian Science Congress this year I interpret as a very genuine appreciation of public health and preventive medicine as a branch of science. I cannot claim any great achievement in the realms of pure research; the greater part of my service has been devoted to practical hygiene and to teaching sanitary science. In choosing a subject for this address, it is natural that I should deal with matters in which I have been particularly interested. Public health and sanitary science, however, cover such a variety of matters that I have thought it better to give some general reflections on medical science and particularly public health work, rather than on any set subject.

In what follows I have given some of the qualities of mind, outlook, and belief which I think should inspire

the medical man and especially the hygienist. It is a high standard but one not unworthy of our calling.

It would here deprecate the division of the science and art of medicine into categories like curative and preventive medicine. Such distinctions have now become artificial and detract from the unity of our science. When we speak of medicine therefore, we mean the science and art of medicine in all its aspects.

The science and art of medicine has three sides: curative medicine, preventive medicine, and thirdly constructive or conservative medicine, which we term hygiene. Some apply themselves mostly either to curative medicine or to preventive medicine, but real constructive medicine or real hygiene is the business of both sets of workers. If we consider the present position in England, we find that preventive medicine is becoming more and more a function of the general practitioner, while health officers are becoming more and more curative in their duties. At present curative medicine must hold the first place, but the ultimate aim is prevention of disease. As Sir George Newman says, 'It is not the event of death which we can escape but the incidence of avoidable invalidity and premature death. It is the enlargement of life and the increase of human capacity, physical and mental, which we seek to ensure'.

I would like to consider shortly with you to-day the place of scientific medicine in human life, and to consider also some qualities and attributes which, as

scientists and medical men, we should have and cultivate.

Medicine was first born of the reaction of the primitive human mind to certain forces and phenomena of nature. It was closely fused in the beginning with religious feelings. This conjunction was for good, in that it recognised the psychological elements in man. It brought man at once in touch with the mysterious; and the mysterious is still the most beautiful thing we can experience, and continues to be the source of all art and science. Mostly, however, and more especially later in the middle ages of Europe, the conjunction with religion and superstition acted as a hindrance; the sanctity of doctrines and dogmas embracing physical phenomena stifled independent speculation, investigation, and experiment, which we know to be the very soul of science. Later, medicine in common with other sciences broke the bounds of doctrine and dogma; experiment and observation replaced philosophical speculation, and with the appreciation of the relationship of structure to function culminating in Harvey's discovery of the circulation of the blood, commenced that wonderful history of experiment, investigation, observation, and discovery with which you are familiar—the names of Leeuwenhoek, Jenner, Pasteur, Koch, Manson, Ross, and Ehrlich are some of the landmarks on a wonderful road along which we still travel. But in this something was wanting—the human note, the closer application of medical knowledge and science for the benefit of mankind in general. It needed the spirit of sympathy, of humanitarianism, to bring medical science into close touch with the every-day life of the masses of the human race, to clothe the bones of science with life. We owe the beginning of this reunion of real religion and medical science mostly to the sympathetic labours of Sir Edwin Chadwick in 1840 on behalf of the working classes in England, and about the same time to the profoundly religious nature and preaching of John Wesley. Of this reunion was born modern public health and preventive medicine; and the spirit that connected Harvey the experimentalist, Chadwick the legislator, and Wesley the humanitarian is that which inspires us still in our work for mankind's advancement. The preventive medicine initiated by Chadwick in 1840 and placed on a sure basis by Simon in 1875 had for its main object the improvement of man's environment. Since then the boundaries of medical science have been tremendously widened. Health is recognised to be something more than reaction of body to surroundings or the mere absence of disease. Man is a personality and an entity, a combination of body, mind, and spirit. These are not really divisible parts of men, however, but merely the results of analysis, it is the indivisible combination that makes up the man. The conceptions of health now envisage the full development of these powers, physical, mental, and spiritual, of which man is possessed. By spiritual we mean here that part of our mind and nature which deals peculiarly with the highest feelings and emotions, with the enjoyment and appreciation of æsthetic, moral, and ethical values. We may say that we have now three aspects of public health—curative, preventive, and perfective—appertaining to body, mind and spirit. It may be that matter, life, and mind are but different stages or levels of the same activity. Matter is the organisation, life the organism, and mind the organiser. The quantum theory has made us familiar with the idea of widely varying states and conditions arising from different quantal distributions of the same fundamental quota of energy. The development of our modern conception of public health is therefore logical—care of the body, the mind, and the spirit. We have in the past concentrated on the body; at the present day we realise more and more the importance of studying the mind. It is probably true that we cannot have a healthy body without a healthy mind. In the last 20 years we have made considerable progress in psychological study. Without pretending to particular knowledge, I think Adler has struck the most helpful note in the development of this side. Man, he says, has three problems set him by the circumstances

and conditions of life on this earth—occupational, social and sexual; how to find an occupation that will enable us to survive under the limitations set by the nature of the earth, how to find a position amongst our fellows that we may co-operate and share the benefits of co-operation; how to accommodate ourselves to the fact that we live in two sexes and that the continuance and furtherance of mankind depends upon our love-life. Readers of Bernard Shaw will remember how in his 'Back to Methuselah' he pictures a human race of great longevity and high (Shavian) intellect, in which the greater part of the period of tutelage up to 20 years, say, is compressed and spent in the egg. Actually the facts seem to be the very opposite. The human race is distinguished by its long period of tutelage and teachability after birth, and in the higher races this period is lengthened in comparison with the most primitive. As man progresses in intellectual ability it is probable that the period of tutelage will also be lengthened. Logically the period during which man should be capable of using his fully developed powers to the fullest advantage should also be prolonged. Hygiene and other euthenic measures have prolonged the average length of life in many countries, but too much importance has perhaps been attached to mere length of years. Expectation of life has meant in too great a degree expectation of bodily life. It must include lengthening of the 'expectation of mental powers' as well; otherwise, the gain will be illusory. The part that medicine along with other sciences will play in the care and development of the spirit is for the future, but it will be more and more closely concerned with man in the development of his higher qualities and aspirations. To quote General Smuts, 'It is here that science ranks with art and religion. In its pursuit of truth, in its vision of order and beauty, it partakes of the quality of both. More and more science is beginning to make a profound æsthetic and religious appeal to thinking people'.

Over 2,500 years ago a Greek poet wrote:—

'Who'er can know
As the long days go
That to live is happy
Hath found his heaven.'

The Greeks, like the Hindus, emphasised certain aspects and attributes of nature, clarifying their thoughts and ideas by the conception of a presiding deity, who in the minds of the common people gradually became anthropomorphosed and an object more of fear and propitiation than a guiding principle. Certain cults in philosophy were thus engendered, each appealing and ministering to one of the many sides of human nature and human feeling, none of them true or complete in itself, but each true and satisfying within its own limits and each part of the larger unknown completeness. The words I have quoted are from a play showing the effect of 'orphyic' philosophy on the human mind. This cult insisted on and emphasised the essential and inherent beauty and sacredness of all life in nature. It is perhaps essentially a philosophy of the present, that here and now is happiness, that our existence in this world is the only thing we shall ever know, and even if it is all that we as individual creatures shall ever know, it should in itself alone be a sufficiency. It is good to be a part of life. Life only knows that it is living; it can never know that it is dead. Mortality of human mind and body in this outlook need not be regarded as any impediment to appreciation of the highest beauty in nature.

As Mimnermus said:—

'All beauteous things for which we live
By laws of time and space decay
But oh, the very reason why
I clasp them, is because they die.'

I cannot quite fully understand those who say that they can see no meaning in human life if it is mortal, if this life after death is not to be followed by an eternal hereafter. This seems a policy of despair and disappointment, a confession of lack of appreciation of

the wonders of nature revealed daily to our senses and to our higher faculties.

Dissatisfaction with existence is the result of individual or collective disappointment—a disappointment to which disease has in the past been largely the cause. National fatalism has been bred of epidemic disease. When mankind has banished or controlled disease and lives the normal span of biological existence, the individual should no longer look on death as a spoil sport but as a natural phenomenon. The desire for immortality will not be so insistent. It is a mistake to regard death itself as an evil. In the fullness of years, it is as natural an event as birth. Goethe wrote very truly. 'The spectacle of nature is always new for she is always renewing the spectators. Life is her most exquisite invention, and death her expert contrivance to get plenty of life'. The only real objection is to premature death, so distressingly common.

These ideas have attracted me for many years—that in mortal human life and existence, physical and mental, we have now nature's highest achievement, that, so far as we can see, it is nature's purpose that human life has, or should have within itself, the possibilities of complete satisfaction and happiness; that the preservation of human life, the protection and betterment of the human germ plasm, the mitigation and ultimate removal of the hindrances that beset the path or what we take to be the path of man's biological development and fulfilment, must be fundamentally correct objects of work in life, which should bring satisfaction and inspiration to the worker and benefit to his fellowmen. These aims are in large measure those of preventive medicine, and it is to those who are devoting their lives and energies to this work that I would speak with hope and encouragement. The care and preservation and improvement of human life form one of the highest ideals of work.

The thinking man at some period of his life puts to himself or has thrust on him questionings of the purpose of life, and on his own answer to himself depends his outlook on life, his career, the ordering of his actions, and his life and his relations to his fellowmen, and his bequest to posterity. There are many answers; wealth, power, happiness, peace, security, service, the avoidance of the disturbing and the distressing; and the resultant of these in the intellectual and thinking portion of a nation determine its character and its progress.

In common with many, my own conviction is that in the quest and appreciation of truth and beauty in their largest sense and meaning, lie the best answer to life's purpose, the one that gives the greatest satisfaction. Einstein says, 'To ponder interminably over the reason for one's own existence or the meaning of life in general seems from an objective point of view to be mere folly; and yet every one has ideals by which he guides his aspirations and judgement. The ideals which have always shone before me and filled me with the joy of living are goodness, beauty, and truth'.

Religion and philosophy we would expect to give us helpful and definite answers to our important questionings. Formal religion however by its insistence on human immortality and a 'soul' entity and on formality of ritual and dogma has failed to satisfy the needs of modern thinking man, while philosophy has guarded itself round with too many abstractions to come into every-day life. For the pursuit of truth we look to science, but it is the poet who helps us most in our appreciation and search of the beautiful. It is not surprising therefore that our profession of medicine has enriched the world in art, sculpture, and poetry, and two of them, John Keats and Robert Bridges, have given us perhaps the most notable contributions in the English language, exemplifying the eternal principle of truth and beauty in life. Keats, the consumptive medical student who died at 26, should be one of the most valuable possessions of the doctor. In spite of the shortness, the sadness, and the tragedy of his life, Keats was able to proclaim that beauty at any rate is real and lasting and that a belief in beauty is the one thing needful in life. 'A thing of beauty is a joy for ever'

is an expression that has almost passed into our every-day life. He held that beauty was the strength which always conquered. He was no sentimentalist—no one ever looked fate straighter in the face than Keats.

.....'For to bear all naked truths,
And to envisage circumstance all calm,
That is the top of sovereignty.'

'Beauty is truth, truth beauty' he wrote and in the essentially mutual identity of the two, lies the unity of science and art, the bridge which joins and unifies intellect and emotion, mind and spirit.

Bridges was a qualified doctor who lived a full life, and at the age of 86 wrote 'The Testament of Beauty'. In this he recounts the conclusions of a lifetime of industry and creation. Man's happiness, he tells us, is his living response to the wealth of nature. Beauty is the prime motive of all his excellence.

Life seems so full of contrasts and antagonistic elements. With nature so inexhaustible of beauty, why is there so much of ugliness; with so much that is noble and fine in civilisation, why is there still so much misery, want, disease, and vice?

We know now that what we call matter is a state of harmony between two essentially different but mutually attractive states—the proton and the electron. The study of the atom shows us that the essence of ultimate structure in nature is the existence of opposites—opposites of like and unlike, of repulsion and attraction which acting together produce equilibrium, create cosmos out of chaos, and harmony out of disorder in obedience to law. In life and civilisation we have similarly states, impulses, motives which though essentially of the same class are nevertheless of the opposite sign as we might say. We have for instance on the one hand the instinct of self-preservation in the individual, a complete selfishness in many ways; and on the other, love, self-abnegation, and sacrifice; in civilised life we still have the fierce competition for existence which leads to intense nationalism, jealousies, tariffs, and wars, and on the other hand, there is a growing feeling of the unity of the human race. Nature shows how matter and life itself are harmonious adjustments of opposite entities; in the study of constitution and behaviour of the atom there is probably much we can learn of application to the larger aspects of life, individual, social, political, and international. Bridges tells us:—

'Love from whom the world begun
Hath the secret of the sun
Love can tell and love alone
Whence the million stars were strewn
Why each atom knows its own
How in spite of woe and death
Gay is life and sweet is breath.'

Symbiosis and parasitism are two natural processes which have immense significance for the public health worker. They have been confused in the past but are really definitely different conceptions. By symbiosis we mean the interdependence of all forms of organic life; by parasitism is meant the absolute dependence of one species on another. In symbiosis we have the basis of mutual assistance and development, and evolutionary progress. It leads to mutual aid and has within it the elements of ethical qualities of sociability and communal life, which lead on to the higher ethical and intellectual developments of man, to sympathy, fidelity, and courage. True symbiosis is beautiful; one has but to instance the diversity of flowers as an example. In parasitism on the other hand we see a degrading influence and a danger of injury, disease, and possible death to the host. There is degeneration and decay in structure and form of the parasite instead of progress. It is a departure from healthy competitive evolution which demands from every organism effort, work, self-dependence, and mutual exchange of service.

Parasitism is sometimes defended by biologists as being an integral part of nature, and one often hears of public health work being considered wrong because it is said to be biologically opposed to nature and an interference with some of her methods. Parasitism is

obviously immoral and a lapse on the part of some of nature's products from her higher and better methods. Parasitism is associated with all that is wrong and unhygienic in conduct, both for the individual and society. Immorality cannot seriously be defended as a legitimate expression of natural instincts. Parasitism is one of the chief, if not the chief obstacle in man's onward progress, and the reduction and final obliteration of human parasites in India will be for some time the main tasks of the public health worker. Tolerance of parasitism by a community or by biologists is an acquiescence in a policy of ignorance and dangerous degradation, if not actually an encouragement of immortality in nature.

At the same time one cannot deny that these degenerated types are just as successful products of adaptation and evolution as are what we call the higher types. In fact evolution has tended more often in the direction of what we call degeneration than in upward progress. If, as I think we must, we accept mind as represented in the human being, as essentially a product of evolution, we see how it may be possible for man to control his own evolution to some extent. In this he is unique. What form of control this will or may take, it is impossible now to say for it would appear unlikely that mind has played any important part in guiding evolution up to the present. Eugenics and population control in a wide sense suggest themselves but as Haldane points out we have been accumulating the knowledge necessary for the guidance of our evolution only for a single generation. Modern studies of heredity and genetics have revealed the extraordinary part played by the 'genes' which make up the structure of the chromosomes of the reproductive male and female cells. Chance mutations in the 'genes' produce changes in inheritable characters. Such changes when useful become permanent by natural selection. Biologists have now succeeded in producing changes in inheritable characters by physical and chemical means. The most remarkable experiments in altering the character of the 'genes' in the reproductive chromosomes are those of Harrison and Muller. The former by feeding ordinary light-coloured moths with chemicals was able to alter the pigment gene so that a true breed of black moth was obtained. Muller by X-rays and radium emanations changed fundamentally the 'genes' of the fruit fly in various ways, so that inheritable and permanent mutations were obtained. The suggestions of such experiments are far reaching. The power to change characteristics permanently is apparently a fact, but the changes cannot at present be foreseen or chosen. When man discovers how to change his characteristics in a desirable direction, he will become a master of evolution and produce human beings with finer minds and bodies who will be able to accelerate these first advances towards the human control of evolutionary destiny. Such control, if it is ever possible, is for the very distant future. At present, such ideas are mere speculations, and for many years to come it would appear that the evolutionary possibilities of man will depend on the same factors as for other species, namely, the plasticity of his germ-plasm and environmental pressure; in other words on chance recombinations and new mutations of the genes of the reproductive chromosomes, and on a modified natural selection. In the meantime, the abolition of parasitism is one at any rate of our immediate tasks.

The instinct and desire for truth and beauty is no sentimental idea which lies only in the domain of artists and poets. It is true that the poet and the artist can best interpret beauty and show it to the ordinary man, but it is really the dominant note in all our lives. The child instinctively seeks it, it fills completely the vision of the adolescent, it dominates the selection of the mate, and guides the parent in the teaching of his children, it is the surest rock of satisfaction and contentment to the middle-aged and the old. Its seeking and its attainment give us true 'culture', give life a meaning, an object, a sense of achievement and satisfaction. Without it and without the sense of its

ultimate reality and importance, many human lives are dull, meaningless, and materialistic, and many human beings disappointed and discontented. As one of our leading psychologists says: 'This search for beauty is not a meaningless search. Our æsthetic emotions are always based on a feeling for health and for the improvement of mankind. All our functions, all our abilities, are formed in this direction. We cannot escape it. We know as beautiful those things which look towards eternity, those things which are for the benefit of mankind and for the future of mankind, the symbols of the way in which we wish our children to develop. This is the beauty which is always drawing us.'

Our profession has very great advantages denied to most others—it leads us to the study of nature and man. The study of nature takes us straight to the spring of all knowledge and life; the study of man leads us to consider nature's highest achievement, a study to which we are devoting the best part of our lives. We should look at nature, not as something that provides us with a little chemistry and botany and physics but as the author of our universe, our earth, our race, and our lives. We should regard man not so much as an individual but as an integral part of nature, an interpretation of her highest motive, as a link in a chain of supreme design. Everything in nature will thus become

..... 'Symbols divine

And manifestations of that beauteous life
Diffused unseen throughout eternal space.'

The capacity and desire for the study of nature and man are themselves the reward of thoughtful life—we feel more clearly our relationship to life and nature, for the mystery of man is probably the mystery of nature.

Wordsworth's lines are familiar but can bear repetition:—

'I have learned to look on nature not as in the hour
Of thoughtless youth, but hearing oftentimes
The still sad music of humanity
Not harsh nor grating.....and I have felt
A presence that disturbs me with the joy
Of elevated thoughts, a sense sublime
Of something far more deeply interfused
Whose dwelling is the light of setting suns
And the round ocean and the living air
And the blue sky, and in the mind of man.'
..... 'Nature never did betray—
The heart that loved her; 'tis her privilege
Through all the years of this our life, to lead
From joy to joy, for she can so inform
The mind that is within us, so impress
With greatness and with beauty, and so feed
With lofty thoughts, that neither evil tongues
Rash judgements, nor the sneers of selfish men
Nor greetings where no kindness is, nor all
The dreary intercourse of daily life,
Shall e'er prevail against us, or disturb
Our cheerful faith, that all which we behold
Is full of blessings.'

Planck, the celebrated physicist, considers that the study of nature fosters the two noblest impulses of the human mind—enthusiasm and reverence.

Our instinct for truth and beauty sends us to nature, and one of our strongest responses to nature is to make us listen to the 'still sad music of humanity', to awake our sense of pity with human aspirations, human suffering, and human needs. Pity is one of the strongest forces behind public health work and preventive medicine, and without it the hygienist and his work will be dull and mechanical. Pity should not stop at sympathetic contemplation, but be translated into vigorous action. In the hygienist the spirit of pity for mankind must be exalted into a moving principle. It is the mainspring of public health energy, and the well of our enthusiasm. It is the force that battles against the strong, against conventional sanctions and accepted gods, against the tyrannies of custom and prejudice. It was the driving force within the new humanitarianism of the 19th century, the force that in the hands of Wesley and Chadwick broke the selfishness and the

indifference of the educated classes of England in the early days of the 19th century. Pity was thus the corner-stone of man's collective health, the structure laid so securely by these two pioneers. It has however the defects of its qualities. 'Pity is of its nature combative, it may outrun discretion and reason, and have an unreasoning contempt for consequences, and counting of costs. It may engender a spirit of recklessness, impatience of opposition, and even fanaticism and ruthlessness.' The hygienist must keep the golden mean if he can, but better sometimes a little recklessness than a placid acquiescence in opposing circumstances.

Of the very essence of pity are bred unselfishness and sacrifice, and in the hygienist these are essential qualities. Without them he will be a disappointed man, his work will lose sanctity and grace, become mechanical, and often ill done or scamped. From them however comes the satisfaction of good work well and faithfully performed in obscure places; for the material rewards of public health work are small, and reputation and fame come to few.

The life of a medical man, general practitioner or hygienist, is essentially one of curiosity. We spend our days finding out things and passing judgement on them, and translating our reasonings into actions, ordinary though the latter may be. In some the instinct of curiosity is highly developed and the search for truth becomes a passion and a purpose. We may be all research workers in a sense but it is only very few of us who have the flair and aptitude for original work. The real research worker is one of the most valuable assets of the medical community and should be encouraged in every way.

Research is not a mere matter of knowledge, nor necessarily of industry, and its results cannot be bought. It cannot be produced by any human machinery however industrious and deserving. It is like poetry; many may write rhymes but few have the real gift of poetical feeling and expression. Shelley said, 'A man cannot say "I will compose poetry"'. The greatest poet even cannot say it for the mind in creation is as a fading coal, which some invisible force like an instant wind, awakens to transitory brightness'. So with research—it needs the natural urge and aptitude, it needs the long apprenticeship in technique and art, untiring industry, the highest self-criticism, but above all, it needs the passion for beauty, the living coal which can be made to glow and produce the golden ore. 'Some have digged deep, yet glanced by the Royal Vein, and a man may come into the pericardium but not the heart of truth.' How many of us who undertake research have the necessary qualities, the divine afflatus? Very few we must honestly admit and perhaps there are too many of us who dabble at it; it might be better if we left the real work to the favoured few, but the dominant instinct of creation is so strong in us that we cannot deny ourselves the joy of producing even a little thing of our very own—'a poor thing but mine own'. The joy of creation is akin to that of the poet. Bridges wrote:—

'I love all beauteous things
I seek and adore them
God hath no better praise
And man in his hasty days
Is honoured for them.
I too will something make
And joy in the making
Altho' to-morrow it seem
Like the empty words of a dream
Remembered on waking.'

This is the true spirit of the research worker.

Another quality the public health worker needs, and needs always is courage; courage that is born of belief and faith in one's work, of a life spent in the study of nature and in the quest of truth and beauty. We need it always for there is sometimes a sense of discouragement if not of actual disapproval in the atmosphere of our work. It is strange that this should be so but it

is a factor to be definitely reckoned on in public health work. Let me remind you again that in the development of public health there have been two distinct ideas. Earlier pioneers like Chadwick and Simon placed the improvement of man's environment as the first essential to his health—and they were then right; but further knowledge proved it was not the only essential. Bacteriology showed that environment though very important in its influence on bodily and mental development, was only the vehicle of disease; it passed on microbial disease from man to man; man was in most instances the host and reservoir of his own diseases. The study of man was the next step. Ignorance, bad habits in old and young, faulty nutrition, etc., could engender disease and ill-health in the best of environments. Education, guidance, and more co-operation between the public and the medical profession are some of the modern trends of public health. These clearly demand something from the ordinary human individual—things which he cannot buy and which cannot be gifted to him. Thus the indifference and sometimes active opposition of the individual adds to the task of the modern hygienist. There is a difference of opinion at present as to how far it is justifiable in these matters to interfere with the liberty of the individual. We can point to instances where compulsory vaccination banished smallpox, but there is the example of the U. S. A. and prohibition to show us that public morality by compulsion in one direction may lead to definite dangers in another. To take the case of India—vaccination is compulsory only in about 7 per cent. of the population; but there is considerable evidence to show that vaccination is as well carried out in those areas where it is voluntary as where it is compulsory; and smallpox has since 1880 been reduced in mortality from 2.12 per 1,000 to about 0.16 per 1,000 all over India. There is a growing feeling at present that in public health policy too much compulsion is undesirable and should be kept rather for times of emergency and extraordinary danger. Indifference, ignorance, and conservatism on the part of the individual are definite handicaps to the health worker; so is the idea that health is the affair of the sanitarian only and not the personal business of the community.

There is another line of criticism which appears particularly in times of stress. I refer to what is familiarly known as the 'population problem'. It is stated that in many countries and in India in particular the population has increased and is still increasing at a rate beyond its means of adequate sustenance. Consequently and inevitably, economic stress, unemployment, malnutrition, and disease, if not worse things must ensue. Unfortunately discussions on this problem have very seldom been free from religious bias, from prejudice and sentiment, and from personal, professional, and class interest. Distinguished scientists, astronomers, and clergymen, and in particular biologists have too often used the prestige of their profession and their own personal distinction to weight their arguments. Granted the truth of these, the remedies suggested have often been hasty, superficial, and class-selfish. Some would lightly welcome disasters like floods and widespread epidemics amongst the general masses; but these need not be taken too literally. Limitations of public health work, especially child welfare work, and the wide adoption of methods of birth control are common and serious suggestions that have been made. The subject is so important that I think a free and honest discussion on the following lines would help greatly:—

(1) What evidence is there that numbers alone are the cause of general economic stress. Is it possible to determine when sufficiency of population passes into over-population? We might bear in mind for instance that in England human life has now been rendered increasingly tolerable to a population rising to 40 millions in an island where a century ago 14 millions had found it hard to earn a livelihood.

(2) How far have methods of population restriction alone been the cause of population adjustments?

(3) Is it desirable that the State give facilities for instruction to the general population in methods of birth control (a) for purely medical reasons in special cases, (b) for economic reasons generally? If desirable, are these feasible?

(4) What would be the effect of attempts at such a movement as the latter on the rural masses of India?

On many of these I have an open mind, but when I consider what humanitarianism and science working together have done for human welfare, I cannot believe that to discourage or curtail medical and public health work at any point—antenatal, natal, in infancy, in childhood, or in adult life can in any way be right.

I may be permitted to make one or two general observations on the subject.

Life of all sorts has been and always will be competitive. The population problem in some form or other will always be with mankind. Methods of prudence come with education, with a rise in the standard of living and a heightened sense of responsibility, and there is a considerable amount of evidence that such methods have now begun to be used extensively in the middle classes of India. Those who strongly advocate the wide adoption of such measures are probably activated by a sense of apprehension of personal or class calamity owing to increasing numbers of the so-called lower classes or races, and by a desire for personal, class, and race security. This apprehension and this desire are psychological phenomena much commoner in the educated middle-aged adult than in youth or in the more elementary human masses. The desire for security is a manifestation of the instinct of self-preservation; it is not however an attribute of youth but of middle age, and may be a danger and a hindrance to real progress of the race and detract from the zest of life. Is our present civilisation getting middle-aged, and are its communities seeking for security in every possible way?

After all, the things desirable for happiness in the ordinary man are simple—food, shelter, health, love, and work. 'Courage, hazard, and hardship and sacrifice can give a quality to human happiness undreamed of by those who sit secure in Zion.' Those who put too great a value on security may have to make way for those who do not. The old Titan gods were displaced by a younger race of gods more adventurous than they:—

'So on our heels a fresh perfection treads
A power more strong in beauty, born of us
And fated to excel us, as we pass
In glory that old darkness.'

We should remember that our stability is but balance, and conduct lies in masterful administration of the unforeseen.

I have indicated in some way what I consider should be the attitude of the medical man and specially the practitioner of preventive medicine towards his science and his work. A constant desire for truth; an appreciation of the beautiful, and of the essential reality and unity of these two; a spirit of sympathy and pity for the human race; continuous assiduity in the alleviation and prevention of disease; a belief in the possibility of upward progress of mankind through evolution controlled by intelligence, and in the application of the ideals of preventive and constructive medicine in the development of man's higher attributes; a spirit of conviction and courage in the face of difficulties.

In conclusion, gentlemen, I would remind you that we meet here with the intention of mutual benefit, of giving the results of original work, of original ideas, of presenting problems, of asking for and helping in giving indications for progress.

'What cheers us most is still the cry
Of those who look for larger sky
And find with every cloud withdrawn
Fresh promise of an ampler dawn.'

Only the best and most talented and industrious of us can push aside the clouds, but all of us can keep on looking and learning. Medical life is surely therefore one of the best and most satisfying and interesting. One of the great attractions of science is that it is limitless and will probably always be somewhat of a mystery.

'Remember that in that inner world to which great literature, science, and art belong, a man may go on all his life learning to see, but he can never see all that is there, he can only hope to see deeper and deeper, more and more, and as he sees, to understand and to love.' In this spirit, gentlemen, I commend to you the science and art of our profession and specially the meetings of our own section of Medical and Veterinary Research.

ALVARENGA PRIZE OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

THE College of Physicians of Philadelphia announces that the next award of the Alvarenga Prize, being the income for one year of the bequest of the late Señor Alvarenga, and amounting to about three hundred dollars, will be made on 14th July, 1933, provided that an essay deemed by the committee of award to be worthy of the prize shall have been offered.

An essay intended for competition may be upon any subject in medicine, but must be accompanied by a written assurance from the author that it has not appeared previously in print, either in whole or in part, in any form, and has not been presented elsewhere in competition for a prize. The essay must represent an addition to the knowledge and understanding of the subject based either upon original or literary research. It must be type-written, and in English acceptable for publication without necessity for editing by the committee. Any illustrations should be appropriate and correctly annotated with the text. Essays must be received by the secretary of the College on or before 1st May, 1933.

Each essay must be sent *without signature*, but must be plainly marked with a motto and be accompanied by a sealed envelope having on its outside the motto of the paper and, within, the name and address of the author.

It is a condition of competition that the successful essay or a copy of it shall remain in possession of the College; and that it may be published by the author with the consent of the College; other essays will be returned upon application within three months after the award.

No award was made for the Alvarenga prize for 1931.

TRAINING IN RADIUM THERAPY

Two clinical assistantships (unsalaried) are available from time to time at the Holt Radium Institute, Manchester. Appointees (male or female) will be expected to remain for a period of not less than four months on a whole-time basis. Appointees will be required to take part in the routine work of the Institute and will receive a practical training and considerable experience in all aspects of radium therapy. The Institute controls three and a half grammes of radium, and has a whole-time trained medical staff.

Candidates must have had either previous surgical experience or a diploma in radiology. Applications should be made to the Director.

TANUKU MEDICAL ASSOCIATION

THE last meeting of the Tanuku Medical Association for the year 1932 was held on Sunday, the 4th December, with Dr. G. Siva Ram, M.B. & B.S., in the chair. The Association placed on record its deep regret on the premature demise of Rao Saheb Dr. M. Seshadri Reddi, L.M.S., who was one of its members, and also resolved to communicate the same to the members of the bereaved family.

Dr. Ch. Sathivasu, M.B. & C.M., M.R.C.S., and Dr. Y. Suryanarayana Rao, L.M.P., were unanimously elected president and secretary of the Association, respectively, for the year 1933.

Dr. G. Siva Ram gave an interesting discourse on the principles of the Ayurvedic system of medicine, which was followed by some discussion.

THE INTERNATIONAL ASSOCIATION OF HOSPITAL SPECIALISTS

THE International Hospital Association organized from the end of September to the beginning of October of last year a series of international post-graduate courses on hospital technique at the Frankfurt a.M., Municipal Hospital, attracting a large attendance of superintendents, physicians, matrons, architects and engineers, coming from 17 different countries. More than 30 internationally-known specialists delivered lectures on important problems; lively discussions followed.

The lectures on kitchen management, hospital linen and laundry have been published—together with interesting articles by other authors—in the October issue of *Nosokomeion*, the official organ of the International Hospital Association.

From June 28th to July 3rd, 1933, the Third International Hospital Congress will meet at Knocke s/Mer, on the Belgian coast. The study committees of the International Hospital Association will submit their reports to the Congress. The discussions will enable the Congress to draw the outlines of practical conclusions having an international value. A five-day study trip to the Netherlands will follow the Congress.

FIFTY YEARS AGO

(From the *Indian Medical Gazette*, March 1883)

THE views regarding the etiology (of enteric fever) more generally accepted in Europe are as follows:—Some organic or animal, especially faecal, contamination of the air or water is looked upon as an essential factor, but the poison is regarded as of a specific nature, and even capable of imparting its character to other faecal matter.

It is not at all necessary, however, to resort to such a view when we recollect the time during which patients are ill, the number and bulk of the stools passed daily (every particle acknowledged to be capable of exciting the disease in others) and the frequency with which these are allowed to pass into the water consumed by others.

It is true that all the outbreaks of this disease in England have been attended by foul health conditions, such as bad water-supply, absence of drainage, or soakage of sewage from cesspools into wells and the like; not unnaturally therefore there has been a tendency to attribute a prime importance to these conditions in the spread, and possibly also in the origin of this disease; and decomposing sewage has been held to be even capable of generating the enteric poison under certain conditions. A community may, however, go on drinking sewage-contaminated water for years, as pointed out by Dr. Ballard in the instance of the village of Nunmay (Somerset), and only suffer from enteric fever when the disease is imported by a patient suffering from the disease. This shows that something of a specific nature, in England at any rate, is necessary to give rise to the disease.

The history of enteric fever is wholly inexplicable on the pythogenic theory of Murchison, but is decidedly that of a specific disease propagating itself by a specific poison generated in the system. The general belief, is that the disease always arises from its introduction into the locality by a person suffering from enteric fever, and probably in England this is generally the case, for the most common type is the epidemic variety, or true enteric fever.

Cases occur in India where no personal communication has arisen with any one suffering from enteric disease, no sanitary defects are discoverable, the dry earth system works well, the surface drainage is good, and so on. This happens not seldom but very frequently, and is in India the rule rather than the exception.

Troops going out to India don't suffer on the march or voyage out, only in April or May following their arrival; if they arrive in October it is absurd to suppose it is dormant all that time, and it is, moreover, impossible that this should be the case with every corps. Importation then is practically out of the question here.

The causes generally assigned as generating enteric and other fevers are completely inadequate to explain the outbreaks in India. Filth, imperfect sewage removal, and decomposing organic matter are ever present in many places in India, and perhaps also in many other countries, but although the filth is permanent, the disease said to be caused by it is not so; and people live and thrive in the midst of it for years perhaps, without ever a case occurring. This I should think was sufficient to prove that something more than filth was necessary for its production, and if the disease was once introduced how should it disappear until all this filth was removed.

This is one great fact not easy to get over in the theory of the septic origin of fevers; something specific is necessary.

Current Topics

Enuresis Among School Children

By R. J. BATTY, M.B., B.Sc., D.P.H.

(Abstracted from the *Medical Officer*, Vol. XLVIII, No. 13, 24th Sept., 1932)

ENURESIS is a fairly common complaint among school children, and it is a source of considerable worry both to the teacher and the parents of the patient. In some Lancashire schools more than 5 per cent. of the children are affected with this complaint, which is sometimes regarded as so trivial that the mother is told not to worry as the child will grow out of it. Unfortunately this prognosis is justified in only a small percentage of cases which remain untreated, and I was impressed by the large number of cases where the complaint had been established for a number of years. Not infrequently it persists into adult life and seriously restricts the adolescent's chances of employment.

Treatment.—Education is of the utmost importance; everything else is only auxiliary treatment.

The usual methods of education—to teach the child to empty its bladder at meal times, at playtime, before going to bed and also immediately it awakens—are too well known to need further elaboration. But the child should also be awakened for urination about 10 P.M. each night, and also as soon as the parents rise each morning. The important point is that this training should start quite early in the life of the infant—certainly not later than the first year.

Before any specific drug treatment is started, all co-existing defects should be put right if possible. In 21 cases I was able to get the patients to undergo an operation for removal of tonsils and adenoids, and in seven cases this measure alone cured the bed-wetting. This gives an operative cure rate of only 33 per cent., but the proportion compares favourably with the results obtained by the usual popular remedies.

Of drug treatment, anthelmintics form the most successful remedy. Threadworms are a prolific cause of bed-wetting, and it is impossible to cure enuresis in such patients until the worms have been eradicated. I

have found Butolan (Bayer), i.e., P-oxy-diphenyl-methane-carbaminate, the most effective anthelmintic. It is put up in the form of $7\frac{1}{2}$ grain tablets. Half a tablet three times a day after meals is sufficient for most children and results in copious evacuations of thread-worms in the stools. It should be combined with a simple purge given every other night and followed by a saline enema the next morning. Frequently it will be found that the whole family is infected with worms, although only the one patient has enuresis as well. Hence, every member of the family should have the stools examined for the presence of worms and treatment must be carried out where necessary. Failure to do this will only lead to eventual disappointment at frequent relapses in the original enuretic patient in the family, through re-infection with worms.

During the past hundred years, belladonna has had the reputation of being a specific in enuresis. The usual advice given is to push the dosage until the child is on the verge of belladonna poisoning. Such treatment, however, only makes the misery of the little bed-wetter more acute. A child with dilated pupils cannot study and will have an unhappy time at school while undergoing intensive belladonna treatment. Further, if any co-existing defects (worms, for example) have not been put right a relapse into bed-wetting is certain as soon as the belladonna is withdrawn. Moderate doses of belladonna act equally well, in my experience, if given over a prolonged period in purely functional cases without co-existing defects.

Space does not admit of a description of every other drug which has been tried.

With regard to psycho-therapeutic methods, simple suggestion acts best of all when removal of co-existing defects has failed to cure. It is the quickest and cheapest of all methods of treatment. The results are usually dramatic, and the gratitude of the parent is correspondingly great.

The Domestic Treatment of Insomnia

By LEONARD WILLIAMS, M.D.

(From the *Medical Press and Circular*, New Series, Vol. CXXXIV, No. 4876, 19th October, 1932, p. 312)

IN furtherance of the endeavour to cultivate therapeutic common sense, to which I have devoted a good deal of my professional life, I have on more than one occasion made so bold as to indulge in the generalisation that the problem of sleeplessness may be reduced to a mathematical equation, thus: insomnia = dyspepsia. When, as in such a case, an attempt is made to explain a condition which is no more than a symptom, by praying in aid another mere symptom, the situation would seem to demand a good many saving clauses and footnotes. I do not propose to indulge in any such, feeling that vagueness is nowhere more permissible than when considering matters connected with sleep, a phenomenon about which nothing is really known.

The type of dyspepsia which is most provocative of insomnia is certainly the hyper-acid or sthenic type. And this is what usually happens: the patient goes to sleep normally, but is painlessly, but widely awakened about 4 A.M., after which sleep is impossible until about 7 A.M. or later, when the desire for repose becomes urgent. The wakefulness during these hours is often incomplete; there is a state of drowsiness in which the spectres of all the disagreeable and horrible things which have ever occurred to the hapless wight are marshalled before him with ghoulish and gleeful insistence. When this kind of suffering has been in progress for some weeks, the patient shows signs of missing his proper amount of repose, the matter gets on his nerves, and he may even dread the approach of bedtime. It is a curious reflection that this drama, which if allowed to continue, may easily become a very serious tragedy, can be checked and cured by so simple an expedient as a few doses of common cooking soda. Fifteen to twenty grains of sodium bicarbonate in the form of

three or four tablets of soda mint, swallowed with half a tumblerful of hot water on retiring, will very often do all that is necessary in the way of neutralising the gastric hyperacidity; but it is well so to arrange matters that the dose can be repeated at about 4 A.M. if necessary. There are many elaborate preparations on the market for the relief of hyperchlorhydria, concerning some of which I can speak highly, notably bisodol and alkazane; but my present purpose is to emphasise the ease with which the condition can be cured by simple inexpensive every-day household means.

It would not be very difficult to draw a picture of the sort of rake's progress which a dyspeptic victim of insomnia is liable to make if the digestive cause of his trouble is not recognised in its early stages, but I forbear. I might, however, say that he would certainly start with veronal or some equally 'harmless' drug, and pass through 'rest cures' in nursing homes, suffer colonic assaults tempered by diathermy and high-frequency, drink waters at foreign spas, and compare symptoms at afternoon tea-tables, until he becomes a confirmed hypochondriac, who is a nuisance to himself and everyone else. And all for the lack of a little imagination, and a dose or two of sodium bicarbonate.

I should not like to leave the question of acid dyspepsia without a word as to two of its causes to which we are less often alive than we ought to be. One is eye-strain; the other, nasal obstruction. These by no means comprise the list, but most of the others are recognised and remembered, whereas these two very often escape. When a suitable alkali is only partially successful in relieving such symptoms as those above described, the refraction of the eye and the freedom of the nasal airway should be carefully tested, and if necessary corrected. Dyspepsia due to eye-strain is really very common.

Still more common, and unfortunately on the upgrade, is insomnia due to tobacco smoking. Whether the sleeplessness of smokers is due purely to dyspepsia, I dare not stop to inquire, though I may say that potent as smoking is in the causation of indigestion of a sly sthenic type, it is probable that the direct effect of the habit on the nervous system has a good deal to say to the insomnia from which sooner or later all smokers suffer. Nicotine, it would seem, differs from most other poisons in the fact it does not, by continued use, establish for itself a tolerance. On the contrary, the physiological tolerance with which we are all born wears itself out sooner or later, and when the limit is reached, symptoms of intolerance appear. I need not attempt to enumerate these; but heart-hurry and coarse tremors will occur to everyone as outstanding examples. Dyspepsia is a very common result of tobacco smoking, but being of gradual onset it is seldom attributed to its true cause. And with the dyspepsia comes insomnia, which, like dyspepsia, begins furtively, and is consequently saddled on to every cause but the right one. I have for many years charged my patients, and those who came to me for life assurance, to give up smoking before intolerance has had time to show itself; that is to say, to cease the stupid, and dangerous, and dirty habit on or before the forty-fifth birthday.

Admitting that the generalisation which ties insomnia to the cart wheels of dyspepsia is too inclusive, and selecting some other causes which may be placed in the same category, I find myself face to face with physical cold feet: a condition which is so generally recognised as to find a place even in many a textbook. The treatment, however, would seem to be so obvious as to require no mention in any of the classics. And yet it is well that the young practitioner should be able to tell his patients with emphasis that there is not the slightest objection to hot bottles so long as they are employed with intelligence. They should be used to warm the foot of the empty bed an hour or more before bedtime, and be removed to a portion of the bed remote from the feet, or altogether ejected, as soon as the bed is entered. This, because of the well-known, but hitherto unexplained, tendency of hot bottles to cause chilblains. Bed socks, too, are very efficacious, and

quite unobjectionable. Bed socks have cured more insomnia in brain workers than all the 'perfectly harmless' hypnotics in the trade circulars. There is another good way of warming the feet, namely, the ventral decubitus, to which I shall return presently. A hot bath immediately before retiring, if not too soon after a meal, is simple and effectual, especially for the occasional insomnia of worry and fatigue. General massage for half an hour before sleep time is very useful, but it has the demerit of being expensive. A fast is an excellent soporific. In one of his letters to Lord Chesterfield, Dr. Johnson signed himself 'Yours Impransus'. I feel sure the philosopher slept soundly that night.

The two ladies who kept house for Herbert Spencer, and related their experiences of the sage in a charming brochure, tell us that he insisted that his bed should be made over a dummy, so that the bed clothes should be comfortably loose to receive him. He had evidently had bitter experience of the obstinacy of chambermaids and nurses, especially trained nurses, who tuck in the bedclothes so tightly that they have to be levered out if anything like freedom is to be possible. The majority of people will tamely submit to these constricted discomforts, thinking that there is something esoterically hygienic about a bed which looks trim and neat. The vice of constriction, from which after all one can kick oneself free, is however as nothing to the vice of overloading with blankets and over-heating generally, which people do not seem to be able to recognise as a cause of insomnia, especially in children. I remember being hauled out one fine summer night to see a child of about three years, who was said to be seriously ill. I found him in a cot drawn up near a large fire; he was clad in flannel pyjamas, almost buried beneath blankets and an eiderdown, and surrounded by hot bottles. Escape from the toils of this foretaste of Hades was effectively prevented by a sort of fishing net well secured at head and foot. Needless to say he was perspiring freely, and was throwing himself about in a vain endeavour to get cool. Except for a slight cough, the most painstaking examination failed to reveal any abnormality whatsoever. So after giving instructions for the child to be given a tepid bath, and placed in a bed with one blanket, in a room with a window wide open, I went home. The next morning I received a message that the patient had had an excellent night and seemed perfectly well. Such in minor degrees, no doubt, but identical in principle, is the explanation of hundreds of cases of sleeplessness, especially in children. And by no means only in children, for over-loading with bed clothes is ridiculously common, almost as common as irrational clothing in the day time, which is admittedly rampant.

Not very long ago I was asked to see a man in a nursing home who could not sleep. My doctor friend assured me that the patient had been examined most carefully from every point of view, but no help towards a diagnosis had emerged. The fact that the patient obtained very little sleep was one to which the nurses would testify. Also there was no doubt that he was losing flesh. When I came to examine him I found it quite difficult to undo the neck button of his pyjamas, and ventured to suggest that this constriction of his neck could account for his want of sleep. The suggestion was not well received, but in the long run it turned out to be correct. In seeking for a cause of insomnia it is imperative that all constriction, however slight, and however seemingly unimportant, should be discovered and removed. I have known the unbuckling of sock suspenders on a railway journey to give sleep to a weary man who was so accustomed to them that he did not realise that he was wearing any.

If you will go into a children's ward when the children are all asleep, you will find the majority of them lying on their faces. When I first observed this and pondered over the cause, I was inclined to attribute it to an instinctive attempt to relieve the heart and great vessels of the weight of the thymus gland, which in childhood is much more considerable than one is inclined

to think. I am still of opinion that such is one of the factors, but I now realise that there are others. One is the drainage of the frontal sinuses; another the relief of the circulation in the pulmonary bases; but the most important is the re-location of the abdominal viscera in their normal quadruped position. Adults are very partially adapted to the upright posture, but children are scarcely at all so adapted; they therefore re-become quadrupeds whenever they get the chance, and nature finds in the long hours of sleep a splendid opportunity of redressing the balance. Why it is that the ventral decubitus should promote warm feet it is difficult to say, but there can be no manner of doubt as to the fact. I have often adopted this position in order to get my feet warm, and have never been disappointed in the result. It may be that the trunks of the large abdominal vessels, being thus relieved of the weight of the ponderous viscera, the circulation of the feet is facilitated. At any rate, whatever the details, it is obvious that the mechanism of the circulation generally is simplified by the ventral decubitus, with great advantage to its efficiency.

Another simple means of assisting the circulation during the night season and thus promoting sleep, is to ensure that the bed shall be at least four inches higher at feet than at head. This brings gravity to the aid of the venous return, with consequent lessening in the force demanded of the systole. Ordinary fracture blocks are all that is necessary, and where these are not obtainable, a little imagination will furnish substitutes. And let it not be forgotten that this inclined plane of the trunk means that the work of the all-important ascending colon is now downhill instead of uphill, an advantage which needs no emphasis.

Drops in the Eyes

(From the *American Journal of Ophthalmology*,
October 1932, Vol. XV, p. 969)

Of the men who lie awake trying to decide whether to operate for a detached retina, or about adopting a certain technic for cataract operations, how many give a thought to the method of putting drops in the eyes of a patient? Yet the latter will be important to one thousand patients for every one who will need either of the operations mentioned; and the drops may affect the success of any operation. The doctor who thinks little about the matter naturally leaves 'drops in the eyes' to the uninstructed nurse or mother. He takes the attitude toward drops, of Dogberry in Shakespeare's play, who says: 'To write and read come by nature'. If it comes by nature, who can expect the doctor to waste his time to teach a mother, or nurse, how to put drops in the eye?

The first drop of the local anæsthetic may decide the success, or failure, of the operation. The dropper, held too far above the eye, the cocaine solution a little too warm, or too cold, the drop strikes the eye with a distinct shock. The patient tense, and the eye full of tears with the excitement, the eye squeezes shut, the bulk of solution goes out of the eye, and there is no anaesthesia. The surgeon, conscious of other operations he must do in the hour, proceeds to inject novocain in spite of the complaints and contortions of the patient; and co-operation necessary for the operation becomes impossible for that patient. Before it is over the surgeon may be in a condition that makes a good operation impossible.

Drops to produce cycloplegia, mydriasis, or miosis must penetrate the cornea and enter the aqueous humor. A grain of atropin absorbed through the conjunctiva has less effect on the pupil, or ciliary body, than if it had been injected into the arm.

To produce cycloplegia, a sufficiently concentrated solution of atropin must remain in contact with the cornea, long enough for the drug to be absorbed into the corneal tissue, whence it will diffuse into the aqueous humor. No amount of it, poured into the conjunctiva to be absorbed into conjunctival vessels and the general

circulation, or run through the lacrimal passages, drying the throat, or causing atropin poisoning, will have the desired effect on the iris, or ciliary muscle. In similar fashion a nurse, putting eserin drops in the eye of a glaucoma patient, may be effectively contracting the pupil, or causing agony from ciliary spasm, according to the knowledge of the effects of eserin that has 'come by nature' to the doctor who prescribed it. If practised like the ritual, which proved effective in bringing 'votive offerings' in Greek temples, before the days of Hippocrates, it may be as useful when practised by a nurse in white uniform, as by a doctor, who has a diploma from a Class A medical school.

To the doctor who is trying to make scientific observations, each drop instilled in the eye is an opportunity to learn something about that eye and the patient; and perhaps something that he has not observed about any eye, or patient before. Observations can be significant, even when one does not have a knife in one hand and forceps in the other. The frequency and importance, even of idiosyncrasy, is worth knowing.

A drop of homatropin solution, placed on the upper limbus, spreads rapidly over the whole cornea and can be watched until it is evenly diffused over the surface. If there is a spasmodic attempt to close the lids, it may be due to shock of the drops falling more than an inch or two, or from the solution being too warm or too cold, or to the neurotic condition of the patient. An acid solution of the drug, or a drop from the wrong bottle, containing an irritating solution, will provoke closure and squeezing of the lids a little later. At least the physician who instils such drops and watches the effects, gets an idea of the efficiency of each application; and can judge better as to the significance of unusual symptoms that may appear, or the number of instillations and time that will be required to secure the maximum effect. It is not a waste of time to become better acquainted with the patient, even if one does not intend to extract a cataract, or make a diagnosis of brain tumour.

Drops are put into the eye for other purposes than to cause cycloplegia; and for each different purpose differences of technic are needed to make the application most effective. If this duty is left to the nurse, or mother, that person should be instructed how to do it. A doctor sent a girl home stating that he wanted the pupils dilated with one per cent. solution of atropin. She returned with the pupils of normal size; and reacting perfectly to light and accommodation; except that one pupil was a trace larger than the other. The bottle of drops was brought along. A drop from this bottle was placed on the upper edge of the cornea, and the upper lid held against the brow for a half minute. In ten minutes the pupil was widely dilated and fixed. In one hour the accommodation was fully paralysed. The grandfather, who brought the child, watched the proceeding with evident interest. Then he said: 'Yes, I put the drops in every time, three times a day. But I did not do it like you did'.—Edward Jackson.

Lead in Urine

By T. C. BOYD, F.I.C.
LIEUTENANT-COLONEL, I.M.S.

and

H. D. GANGULY, M.Sc.

(Abstracted from the *Indian Journal of Medical Research*, Vol. XX, July, 1932, p. 75)

ANALYTICAL METHODS FOR THE DETECTION OF LEAD
Broadly speaking these may be classified into:—

- (1) Chemical methods.
- (2) Micro-chemical methods.
- (3) Spectrographic methods.

A perusal of the current literature will impress the enquirer with the many methods that can be applied to this problem under the heads (1) and (2). In this paper, however, we propose to restrict ourselves purely to the micro-chemical tests and particularly to the

triple nitrite test of Behrens and Kley, in which the presence of lead is proved by the formation of the crystalline compound $K_2Cu Pb(NO_2)_6$ readily recognized under the microscope. Lawrence T. Fairhall of the Harvard Medical School has given an excellent account of his method (Journal of Biological Chemistry, 1923) and we have followed closely his technique in the actual application of the test itself.

GENERAL PROCEDURE ADAPTED

(1) *Collection of the urine.*—This was collected direct where possible into Pyrex flasks which before despatch to the wards were prepared by treating them with 100 c.c. of lead-free hydrochloric acid specific gravity 1.124 and heating on the waterbath for three hours, then subsequent treatment with dilute nitric acid for one hour and finally washing with double distilled water and draining. Officers sending in specimens to the laboratory appear to neglect the importance of clean lead-free containers and possible contaminations from urinals, etc. The urine should also be freshly collected as we find that when fresh it ashes more easily. We need not refer again to the importance of the preparation of the glassware used in the test, nor to the necessity of being certain that all reagents are lead-free.

(2) *Ashing of the urine.*—One litre of the urine is evaporated to dryness in a porcelain basin on the waterbath and the residue completely ashed in a silica or porcelain crucible the former is preferable. The time required to ash the residue obtained from one litre takes about twenty-five hours over the Bunsen flame.

(3) *Fairhall's application of the Behrens Kley triple nitrite test.*—The ash obtained is moistened with distilled water, twenty-five c.c. and fifteen c.c. of pure hydrochloric acid specific gravity 1.124 added, this treatment does not cause complete solution of the ash, a little white gelatinous matter is left undissolved. A few drops of methyl orange are now added as an indicator and excess of acid neutralized with ammonium hydroxide to a final pH of approximately 3.8. Particular care must be taken to adjust the reaction or the lead will not be completely precipitated. The whole is now transferred to a centrifuge tube and freed by spinning from the undissolved precipitate. (We have found that examination of the gelatinous precipitate usually reveals the presence of lead where the final result of the test is positive.) Two c.c. of a saturated solution of ammonium sulphate and a drop of a two per cent. copper acetate solution are now added and the whole saturated with sulphuretted hydrogen for at least half an hour. The precipitated sulphides are separated by the centrifuge and thoroughly washed three times with double distilled water, the final wash water is removed by means of a capillary pipette. The tube containing the precipitate is now placed in a beaker of boiling water and two drops of nitric acid specific gravity 1.140 added followed by two drops of water. When solution is complete the whole is removed and evaporated to dryness on a microscopic slide, when dry 0.005 c.c. of a four per cent. sodium acetate solution is added and evaporation to dryness again carried out. The slide is now allowed to cool at room temperature, when cool the residue is treated with 0.005 c.c. of acetic acid and a small crystal of potassium nitrite. Five minutes are allowed to elapse when the slide is examined under the microscope for the characteristic crystals. The examination should not be delayed too long as we find that in this hot damp climate the crystals are liable to disappear. One other point that requires attention is that when dissolving the precipitated sulphides with nitric acid, the tube should not be left in the boiling water longer than one minute as some of the sulphur is oxidized to sulphuric acid which interferes with the test.

Sensitivity of the test.—Experimenting with known dilutions of lead in water, we found this test to be sensitive to 0.00003 mg., the figure given by Behrens and Kley.

SUMMARY OF RESULTS OBTAINED

Of the twelve cases examined under the European series lead was detected in ten.

Of the twenty-four cases examined under the Indian series lead was detected in two only.

Of the seven suspected Indian lead poisoning cases lead was detected in four.

The difference found between Series I European and Series II Indian is worthy of note.

It is of interest to compare these results with others obtained by workers outside India.

Francis, Harvey and Buchan, *Analyst*, December 1929, p. 725, found that in fifty-five samples of urine examined by them lead varied from nil to 0.133 mg. per litre giving an average of 0.040 mg.

Cooksey and Walton (Office of the Director-General of Public Health, Sydney), *Analyst*, February 1929, p. 97, found in normal urines a lead content of from 0.02 mg. to 0.05 mg. per litre.

Fretwurst and Hertz, *Archiv. Hyg.*, 1930, found in normal urines lead varying from 0.01 to 0.07 mg. per litre and in workers exposed to lead but showing no toxic symptoms 0.02 to 0.9 mg. per litre. Kehoe and others, *Jour. Amer. Med. Assoc.*, 1926, p. 2081, found that normal workmen pass lead in the urine and faeces, and further that there is no diagnostic value in qualitative lead determinations in the excreta of persons suspected of having lead poisoning and at present no quantitative expression of lead excretion in man which may be said to be significant of impending or present lead poisoning.

Edwin Bramwell in an article in the *B. M. J.*, 1931, July 18th, mentions two hundred cases of suspected lead poisoning in the Mayo clinic where one hundred were excreting lead and points out that the presence or absence of lead in the urine is a point to which too much importance must not be attached.

Millet, *Jour. Biol. Chem.*, 1929, LXXXIII, p. 265, points out that the major part of the lead injected in cancer cases is excreted in the faeces and that there is no evidence that the lead injected is excreted in the urine.

In an article by I. A. Christiansen, G. Hevesy and S. Lomholt abstracted in the *Analyst*, 1924, October, p. 490, it would appear that the greater part of the lead accumulates in the liver from where it is slowly excreted in the faeces, and also that considerable amounts are found in the intestines and kidneys.

DISCUSSION

Objections may be raised to the method of analysis employed on the grounds that there may be an appreciable loss of lead in the ashing, loss may also occur in the precipitation process, in addition, from the practical standpoint, it may be urged that the time required for the analysis is too long and that the collection of a litre of urine under supervision especially in a hot climate is difficult. Further the method is not quantitative. We are fully alive to all these criticisms but the object of our investigation was to find out if the excretion of lead was common in this country and, if so, was it equally distributed amongst the different classes of the community. Our results show that amongst Europeans it is extremely common but that where Indians are concerned the amount of lead excreted in the urine falls outside the limit of sensitivity of the method employed. Why there should be this difference we are unable at the moment to explain and can only record our findings.

CONCLUSIONS

We have recorded the result of examinations made on urine for the determination of lead on various classes of the community and as far as Europeans are concerned this appears to be commonly present while in the Indian groups of the community the excretion of this element appears to lie outside the sensitivity of the method employed.

Finally, we have drawn attention to the fact that the views of certain investigators appear to indicate very strongly that the detection of lead in urine, or even its quantitative estimation, is of very doubtful value as far as the diagnosis of lead poisoning is concerned.

Reviews

A MANUAL OF BACTERIOLOGY MEDICAL AND APPLIED.—By Professor R. T. Hewlett, M.D., F.R.C.P., D.P.H., and Professor James McIntosh, M.D., B.Ch. Ninth Edition. London: J. & A. Churchill, 1932. Pp. ix plus 746, with 43 plates and 66 figures in the text. Price, 18s. net.

The ninth edition of Professor Hewlett's well-known textbook of bacteriology has now appeared; this edition was produced with the collaboration of Professor McIntosh whose name appears on the title page for the first time. Although the eighth edition was published only six years ago, it is surprising to note the number of alterations and additions that have been made in this last edition. It has been thoroughly revised and brought up to date, both by the introduction of new matter and by the omission of old matter and less important passages.

Such subjects as the handling of the microscope, the preparation and standardization of media, serological tests, and the bacteriological examination of water, air and soil are fully dealt with. The systematic study of bacteria is all that could be desired and the student will find in this book simple, straightforward and clear accounts of most of the recent work. The section on ultra-microscopic organisms has been extended and a fuller account of virus diseases has been given. Bacteriophage, however, is considered very briefly, only four and a half pages are devoted to this very important subject, and there is nothing to help the student in the study of bacteriophage. The spirochaetes and spirochaetosis, with syphilis, have been separated from the

protozoa, and constitute a new chapter, and a full account of the Kahn test is included. We would have wished for the total exclusion of the chapter on protozoa from a textbook on bacteriology. For the student in the East a chapter of only forty pages devoted to animal parasites such as the pathogenic amœbæ, trypanosomes, leishmania, coccidia and plasmodia cannot be of much value. A chapter dealing with the physiology of bacteria would have been very valuable to the student of bacteriology. This is a branch of the subject which, though of fundamental importance to the proper study of bacteria, has been persistently neglected or insufficiently dealt with in the textbooks of bacteriology.

On p. 388 it is stated that in the East the Shiga strain of dysentery is the predominant infection, and in the West the Flexner strain. This is not in accordance with the findings in India where the majority of the cases of bacillary dysentery are due to the Flexner strains. The only other criticism that we have to offer is that the tables on pages 400 to 405, showing cultural reactions of certain aerobic non-spore-producing intestinal bacilli with the names of bacteria in alphabetical order, would have been better had the bacteria been grouped according to their cultural reactions.

Several excellent new plates and new figures have been added in this edition and have enhanced the value of this book. Altogether this is an excellent textbook and one that may be very cordially recommended to the student of bacteriology.

welfare of the people. In addition there are purely voluntary agencies working on self-supporting lines while others, though independent in control, receive official assistance and grants. The author is insistent that *every* agency should co-operate and that there should be all round co-ordination of work.

Being itself a very condensed compilation from various sources, it is difficult to review the book without practically quoting the whole of it. Mr. Brayne's work in Gurgaon is well known and has been a great stimulus to work in other places, though the work was expensive and has practically died since its promoter left the district. Still it showed what could be done with the villagers of India. The shrewd statement is made that health, agriculture, and veterinary service only appeal to the villager if his life is worth while to him and it is the educationists' task to make him understand how worth while his life might be. We get here to the great difficulty of defining what constitutes human happiness. One point which is brought home is that education in India has a remote and abstract quality about it which more than often defeats its object. Education should have an intimate connection with home life—secondary education in India has very little of this, and the young are not taught to plan their lives in relation to their

own conditions and their own future. The object of rural reconstruction is to educate, but to educate in all directions; the horizon must be pushed back in all directions at once. The various methods of attempts at rural construction are outlined. In the south, welfare centres are used, usually under the auspices of the Y. M. C. A.; in the Punjab and the United Provinces there are official rural community boards, of which a minister is chairman; in Bombay the taluka development associations unite official efforts with the leading citizens of the neighbourhood; the eastern provinces of Bengal, Assam, and Bihar and Orissa are without any definite official department, so-called, for co-ordinating Government and private agencies, though there are a good few of the latter, such as the co-operative anti-malarial societies and women's institutes like the Saroj Nalini Dutt Association. Dr. Rabindra Nath Tagore's rural university stands in a class apart, though it remains to be seen whether it will survive apart from Dr. Tagore's stimulation and inspiration.

The lines of the pamphlet are indicated and it is an important contribution to a subject which every worker here has at heart, namely, the improvement of the lot of the Indian peasant.

A. D. S.

Annual Reports

ANNUAL REPORT ON THE RANCHI INDIAN MENTAL HOSPITAL, KANKE, FOR THE YEAR 1930. PATNA, 1932, SUPDT., GOVT. PRINTING, BIHAR AND ORISSA. PRICE, RE. 1-4.

The following are abstracts from this very interesting report by Major J. E. Dhunjibhoy, I.M.S., the Superintendent of the hospital:—

The accommodation of the hospital remained the same as in the previous years, viz, 1,014 for males and 272 for females, total 1,286, which is apportioned in the proportion of three-fourths, and a quarter to Bengal and Bihar and Orissa respectively.

The male section of the hospital remained overcrowded throughout the year under report but to a lesser degree than in the previous years. The restriction which was imposed by Government on the admission of harmless and non-dangerous male patients in the previous years was also in vogue during the year under review, and only carefully-selected cases who were certified as dangerous and unmanageable at home or elsewhere were admitted, for this 50 extra emergency beds were sanctioned by Government. The overcrowding of the hospital, its causes and the steps proposed to be taken have been fully dealt with in the last Triennial Report (1927—29) of this hospital. Owing to financial stringency none of the additional buildings, included in the scheme of expansion of this hospital which has been accepted by Government, could be taken up during the year under report.

Patients.—The following table shows the number of patients resident in the hospital on the 1st January of 1930 and of the previous two years:—

Years	Male	Female	Total
1930 ..	1,049	215	1,264
1929 ..	1,065	209	1,274
1928 ..	1,160	234	1,394

It will be evident from the above figures that the congestion in the male section has been gradually relieved. On the 31st December, 1930, there were only 1,034 male patients resident in the hospital, i.e., the male section was overcrowded by only 20 patients at the end of the year under report.

In this large hospital there is a large number of chronic, incurable, harmless and homeless patients who were originally transferred from the old hospitals of Berhampore, Dacca and Patna. These chronic and incurable patients unnecessarily occupy the beds and

thus prevent the admission of those patients who really require the immediate attention and treatment of this institution.

I have, therefore, proposed to Government to open a 'chronic' depôt for these harmless and homeless patients, as they can derive no further benefit by their stay in this modern hospital. Such a depôt can preferably be opened in one of the old abolished mental hospitals either in Bengal or Bihar and Orissa.

Special efforts were made during the year under report as in the previous years to discharge 13 chronic and harmless patients to the care of their relatives who could be traced by the magistrates of their districts, as a result of which 10 patients were handed over, and the plea of inability which was put forward by the relatives of 3 patients to take them over was accepted by the committing magistrates and they were, therefore, not discharged.

The following table shows the ratio per cent. of cases cured to the total admissions during the year under report as well as in three previous years:—

Years	Male	Female	Total
1930 ..	23.49	22.22	24.24
1929 ..	16.94	22.22	18.60
1928 ..	30.86	16.00	27.36
1927 ..	30.87	13.20	27.41

Death rate.—The percentage of deaths to daily average strength during the year under report and in the two previous years is shown in the following table:—

Years	Male	Female	Total
1930 ..	2.02	2.29	2.07
1929 ..	1.91	2.39	1.99
1928 ..	3.41	3.66	3.45

The general health of the patients was good throughout the period under report. The daily average number of sick treated in the infirmaries for bodily ailments was 59.93 males, 1.67 females and 61.60 total against 53.95 males, 3.47 females, total 57.42 in the previous year.

Statement VI shows the types of insanity of the patients admitted during the year under report. Mania, melancholia, dementia præcox, toxic insanity and confusional insanity were the principal types treated.

Paying patients.—Seventy-nine patients (60 males and 19 females) were treated during the year under

report as compared with 60 (48 males and 12 females) in 1929. During the year under report as well as in the last two years several applications for the admission of paying patients had to be refused for want of accommodation in the male section.

The scheme for the construction of paying patients' wards has been deferred by Government owing to the financial stringency. In the meantime, the arrangement of keeping the paying patients of the male section in a separate ward of one of the quiet patients' blocks is continuing. A few suitable patients are also given single rooms from time to time when available. In the female section, although there is no separate paying patients' ward, first class paying patients are given separate rooms and other classes of patients are kept in separate wards in the infirmary block. This comfort for female paying patients is possible at present, as there is no overcrowding in the female section.

Suicide.—I am glad to be able to report that there was no case of suicide during the year under report and the previous three years in spite of the fact that there are more than 70 suicidal patients in the hospital, the majority of whom are potential suicides. Several serious attempts were made by potential suicides to end their lives generally by trying to strangle or hang themselves.

It is satisfactory to note that there was no case of serious accident or injury during the year under report in spite of the fact that all patients admitted during the year were sent here as definitely dangerous. There were a few minor accidents and injuries but none were serious. This result can fairly be attributed to the kind treatment meted out to this class of patient in this hospital as already stated in my annual report of 1928.

Treatment of mental conditions.—*Hydrotherapy (prolonged bath).*—During the year under report 69 cases were given this treatment as against 43 in the previous year. The average number of hours of immersion per patient was 146. The result of the treatment was most encouraging. A special hydrotherapy ward has not yet been provided for want of which this important form of therapy could not be more extensively used.

Dietetic.—Special attention is paid to the proper dieting of patients of this hospital as a well-balanced nourishing diet largely helps the recovery rate. The weight charts of the patients showed a general rise throughout the year under report. The average gain in weight per patient during the year under report was 2.00 lbs. per every male patient and 0.85 lb. per every female patient.

Artificial feeding.—Cases refusing food were spoon-fed by nurses and attendants, recourse to artificial feeding being resorted to in the few special cases exhibiting active refusal to food.

We have many stuporous cases of various degree which often require artificial feeding by tube either per nose, mouth or rectum, and I should like to mention one case of benign stupor that was kept alive for 3½ years by nasal feeding twice daily.

Occupational therapy.—This therapy is the sheet-anchor of our treatment in this hospital, and has been carried out as vigorously as before. Patients of both sexes are suitably employed chiefly in gardening, weaving, cane and bamboo work, smithy, carpentry, tailoring, cobbling, mending clothes, mattress and pillow-making, lace-making, knitting, embroidery work, domestic and office work, etc., etc. The patients' labour is fully utilized towards supplying the needs of the hospital. Jharans, dusooti cloth, bandage cloth, asans and many other useful articles required for the hospital are manufactured in the occupational therapy classes. The weaving section in the female section was considerably expanded during the year under report but the progress was hampered for want of a weaving instructress, this post was sanctioned by Government but no appointment was made for want of funds. The vegetable garden of this hospital is entirely run by the patients' labour and the hospital is entirely self-supporting as regards its vegetable and fruit supply.

The average daily number of patients employed in the vegetable garden was 139 in 1930, 145 in 1929 and 142 in 1928.

The construction of four wells in the garden area for the purpose of irrigation was taken in hand during the year under review, by the Public Works Department and the work is expected to be completed in 1931-32.

Drugs.—(a) On my return from leave I introduced what I had seen in Zurich Hospital, popularly known as Zurich treatment. It consists of heroic doses of sodium luminal gr. xii per day given by mouth or by deep intramuscular injections in the buttock. It is continued for over a fortnight. It is very beneficial in cases of acute excitement with intractable insomnia. We tried it in several of our cases of this type and the results were very encouraging but unfortunately the benefit was temporary.

(b) Deep intramuscular injections of paraldehyde. Paraldehyde was also injected daily in the buttocks for a period of a fortnight in highly excited cases. The results were very encouraging but the benefit was temporary.

(c) During the year under review bromo-chloral co. was also prescribed by me to some mild as well as intractable cases of insomnia. In some cases the drug acted like a charm but failed in others.

In fact all the above drugs tried in the way described above during the year under report have come to stay on our register of drugs for insomnia and general excitement.

Organotherapy.—Nineteen patients were treated with different glandular compounds during the period under review but the results were not very encouraging. Thyroid was found to be a very good activating agent when given in large doses for a period of 10 days in acute melancholia and mild stupor cases.

Physiotherapy.—Strictest attention is paid in this hospital to correct all physical defects before an attempt is made to explore the psychological defects. Tonsils, nasal sinuses, adenoids, eyes, ears, etc., are contributory causes to mental derangement when they are defective. Therefore on admission of a patient all physical avenues which are believed to contribute a smaller or larger share in the causation of mental diseases are thoroughly explored.

Teeth.—(a) The services of a whole-time dentist on the staff are desirable but funds have not been forthcoming.

Throughout the year under review and the previous years, Dr. D. R. Choudhury, one of the sub-assistant surgeons on our staff, treated the teeth of a number of the patients.

(b) Similarly, Dr. P. C. Das, M.B., who is happily also an eye specialist, did excellent work with the ophthalmoscope and operated on some cases of cataract among the patients.

(c) **Syphilis.**—During the year under report, 425 blood specimens were sent to the Pathological Laboratory of the Prince of Wales Medical College, Patna, for the Wassermann test and suitable anti-syphilitic treatment was given to positive cases.

(d) **Leprosy.**—During the year under review we were obliged to treat three highly-contagious positive cases of leprosy in the hospital as those cases were not admitted in the Albert Victor Leper Hospital, Gobra (Calcutta), for want of accommodation. This is admittedly a serious state of affairs, which would be remedied if the Government of Bengal could arrange to reserve a few beds for this hospital in the Albert Victor Leper Hospital at Gobra for the treatment of such acute cases. To treat highly-contagious leper cases in a mental hospital is undesirable for obvious reasons.

Malarial therapy.—During the year under review four patients were given malarial therapy with indifferent results.

Sulfosin therapy.—On my return from leave during the latter part of the year under report I have injected a few selected cases with sulfosin (which is 1 per cent. solution or suspension of sulphur in olive oil). Dr. Knud Schroedor, an eminent physician of

Denmark, in 1929, claimed to produce pyrexia by injections of sulphur in olive oil better than that produced by malarial therapy. So far we agree with his claims as our patients have shown a steady rise of temperature up to 103 degrees after every injection. The results of our experiments will be fully given in our next annual report as at the time of writing this report the treatment is still under trial and not yet completed.

Psychotherapy.—A case was admitted from Calcutta as one of complete paralysis of both legs with mental excitement. The patient was brought into the hospital on a stretcher. On examination the case was diagnosed as one of 'conversion hysteria' and the patient, who was treated as a case of paralysis of the legs for three months outside, was made to walk within eight days of his admission and was discharged cured within two months, and he went to Goa—his native place—which is a distance of 1,500 miles from Ranchi.

We rarely see such early cases admitted into this hospital. We are only called upon to treat all chronic cases whose relations and friends have kept them in their homes for years under treatment of every one but a psychiatrist, and who are only sent to us when they become unmanageable and dangerous at home. This is further aggravated by the present unavoidable congestion of the hospital with the result that cases are allowed to remain untreated in jails or houses until such time as accommodation is available. In spite of all these difficulties I am happy to be able to report that our proportion of cures to so-called new admissions as well as to average strength of the total population, can proudly be looked upon as extremely good.

Sports and amusements.—Both indoor and outdoor games were played by quite a large number of patients and they all seemed to take more active interest in the matter. Several football and hockey matches were played by the hospital team, consisting of staff and patients, against several other units at Kanke and Ranchi. Several patients of both sexes played tennis and badminton.

Musical and other entertainments.—In the absence of a proper amusement hall, which is a pressing need of the hospital, one of the dormitories of a quiet patients' block, is utilized for the purpose. Twelve theatrical performances both Hindi and Bengali and several musical soirees got up by the staff and patients were staged during the year under report, to the great enjoyment of patients of both sexes. A few well-known magicians entertained the patients. Besides, the patients of both the sections were entertained by the musical entertainer on every alternate day. Gramophones are played by the patients every evening in different wards by turn. The radio set, which was installed in 1929 out of a special donation made for the purpose by Raja B. D. Birla, was a source of great amusement to patients. The concert party of the hospital which was only organised a couple of years ago played both Indian and English music throughout the year and afforded another source of great pleasure to patients. Its existence and the maintenance of the high standard of music are entirely due to the enthusiasm and perseverance of Sub-Assistant Surgeon Dr. Dhaniraj Choudhury. The band also played at patients' games and theatricals. A few musical instruments were purchased during the year.

Picnics.—During the fine weather large numbers of patients picnicked out on the nearest hills, riversides, gardens, etc., with the hospital concert party. Those outings were very much enjoyed by them.

Parole.—Many dependable patients were granted full 'local' and 'Ranchi' paroles. Others were allowed out both morning and evening for walks with attendants. None of the patients granted parole abused the privilege, and the number of patients on parole is increasing every year. The effect on the health of patients has been striking.

Drives.—Patients of both sexes were sent out regularly by turn throughout the year for motor drives both morning and evening in the hospital cars.

Expenditure.—The total expenditure exclusive of the amount received from the paying patients and miscellaneous receipts was Rs. 5,70,175-4-7 during the year under report as compared with Rs. 7,60,978-7-1 in 1929 and Rs. 6,34,085-1-6 in 1928.

Annual average cost per patient.—The following table shows the annual average cost per head during the year under report and the two previous years:—

Years	Annual cost per head inclusive of Public Works Department charges			Annual cost per head exclusive of Public Works Department charges		
			Rs. As. P.			Rs. As. P.
1930			453 3 0			390 5 9
1929			605 5 3			418 7 4
1928			475 14 3			357 3 2

During the year under report medical students from the Prince of Wales Medical College, Patna, were sent in two batches as in the previous years, for intensive training in mental diseases as required by the curriculum of the Patna University for the degree of M.B., B.S.

The medical and nursing staff of this hospital were also allowed to attend these lectures and demonstrations.

REPORT OF THE DIRECTOR OF PUBLIC HEALTH OF MADRAS PRESIDENCY, FOR 1931. BY LIEUT.-COL. J. R. D. WEBB, O.B.E., I.M.S. MADRAS: SUPERINTENDENT, GOVERNMENT PRESS, 1932. PRICE, RE. 1-2.

Economic distress, diminished incomes and revenues, and the stern necessity for retrenchment in staff, salaries and activities are familiar notes in every annual report for 1931. The present report is no exception. Two first class Health Officers have been retrenched and the Professorship of Hygiene held in abeyance. This is Colonel Webb's first annual report and an air of optimism pervades it which augurs well for the progress of the public health of the Presidency under his guidance.

The population of Madras province in 1931 was determined by Census as 46,740,107, an increase of 4,421,122 over that of 1921 representing an increase of 9.46 per cent. This is the highest rate of increase for the last three decades. Colonel Webb gives some interesting paragraphs on the calculations of birth and death rates in intercensal years, showing the fallacies of determining them on censal populations. The whole of Indian statistics are vitiated in this way and towards the end of intercensal periods, both birth and death rates are much higher than actuals; then in the census years there is a sudden drop in these rates due to the new increased census number being taken as the denominator. We believe the point is being taken up by the Public Health Commissioner with the Government of India. On the new population, the birth and death rates of the province were 35.54 and 23.72 per 1,000. Registration is still deficient all over but there are very definite signs of improvement. As regards disease the year 1931 was a severe epidemic of cholera all over the province. There is a tendency for such a recrudescence every 5 or 6 years and from statistical study an actual increase had been forecasted and certain measures of prevention and protection put in train before the actual increase occurred. As is usual in Madras, the epidemic was most severe during the months of the north-east monsoon, i.e., in the first quarter of the year. Cholera bacteriophage was prepared on a small scale by the Director of the King Institute and given in 17 cases as a remedial measure. It was not tried as a prophylactic. Rs. 3,000 was devoted to an experiment as to the value of bilt vaccine but the results have not yet been analysed.

Improvement of elementary sanitation, i.e., the provision of a pure water supply and the sanitary disposal of night-soil, proceeds but slowly, but in some districts definitely. In one district for instance over 2,000 bored-hole latrines were established.

Malaria is a severe disease in Madras taken as a whole. Retrenchment necessities did away with the temporary malarial establishment. Such anti-mosquito measures as were carried out gave good results. There are some interesting paragraphs on beri-beri and epidemic dropsy. The report does not give the distinguishing points between the two diseases. Colonel Webb adduces evidence that beri-beri is an infection picked up from the soil, and that epidemic dropsy is not due to rice but to mustard oil adulterated with odismari (*Americana mexicana*). A more critical and detailed report on these statements is desirable. The evidence is merely stated and the opinion of the Director of Public Health may be quoted as authoritative.

Glove-oiled vaccine lymph is now being issued from the King Institute and has been found to be very successful. Further trials are being made and reports of these will be awaited with interest. Vaccination (primary) is compulsory in most areas, but responsibility for prosecutions is in many cases being evaded by chairmen of district boards. Fear of unpopularity explains these deviations from responsible duty. Control over district vaccinations is also divided and this does not help matters.

Maternal and child-welfare work is being carefully fostered, and there is an all-time Assistant Director of Public Health for maternity and child-welfare work. Infantile mortality rates are still high (186.6 per 1,000 births). The work undertaken however has necessarily been rather of an elementary character, i.e., the feeding and bathing of children. The principles of proper welfare work are quite thoroughly understood but there are difficulties in the way. Despite the Madras Nurses and Midwives Act of 1926 which requires registration of all trained midwives, there are still hundreds of untrained barber midwives. Maternity and child welfare work is not included in the work obligatory under the Local Boards and District Municipalities Acts. The report also contains that of the Sanitary Engineer to the Public Health Department. This department had dealt mainly with water supplies, of which five new installations were completed during the year.

THE MISSION TO LEPERS. REPORT OF FIFTY-EIGHTH YEAR. AUGUST 1932.

A REVIEW OF THE YEAR'S MEDICAL WORK

The Mission to Lepers is a progressive body—of that, perusal of the last few annual reports leaves little doubt. The 'Asylum', a resort for those without hope of recovery, has given place to the 'Home' and 'Hospital' within the last few years. Some twelve years ago treatment consisted of palliatives alone; the following statistics for the past year tell a very different tale:

Mission to Lepers for India—Statistics of Treatment

Inmates who received treatment for three months and upwards	5,524
Much improved	1,877
Slightly improved	2,023
Inmates who became worse	399
Had to stop treatment or left	759
Cases arrested <i>without</i> deformity	450
Cases discharged <i>without</i> deformity	311
Cases arrested <i>with</i> deformity	337
Cases discharged <i>with</i> deformity	81
Cases arrested <i>without</i> deformity in a previous year, but relapsed during the year	31
Number of out-patients treated	4,418
Cases arrested or became symptom-free (from among out-patients)	29

In many of the institutions the majority of the patients now come with the distinct object and hope

of getting better, and for many of them that hope has not proved a vain one.

Though many of the homes are constantly being enlarged, their accommodation cannot cope with the demand for admission, and one of the saddest duties of the superintendent is often to turn away those who have travelled long days of painful and wearisome journeying, for lack of room.

What strikes one when one visits such Homes as Purulia, Raniganj, Chandkuri and many others, is the look of hope and cheerfulness on the faces around one; the cheerfulness of having daily work to do and being able to do it. The sympathetic organization of labour according to ability to do it is one of the most important parts of the treatment. Leprosy can be treated successfully only by the expert, but the doctor must also be an expert in the treatment of all the scores of ailments which complicate and amplify leprosy if he is to make any headway. Such doctors are not lacking on the staff of the Mission to Lepers in India, and their number and usefulness increases year by year.

But seventy-five per cent. of the treatment lies in the hands of the patient himself, and without his full co-operation there is little hope. It is only by sympathetic and understanding training, often through long months and years, that the patient can be taught to do his part; and this is where the idealism and personality of the mission superintendent, doctor and nurse are most severely tested.

The out-patient clinic in connection with the leper home is a new feature of recent years. Last year four out of every nine cases treated were out-patients, and the numbers would be far larger were the staff available.

Correspondence

PANTOCAIN—A NEW COCAINE SUBSTITUTE

To the Editor, THE INDICAL MEDICAL GAZETTE

SIR,—Messrs. Havero Trading Co., Ltd., were good enough to supply me a one gramme bottle of their new product, Pantocain, for clinical trial.

Pantocain is p-butyl-amino-benzoyl-amino-ethanol-hydrochloride. The makers recommend this drug for anaesthesia of practically every region of the body.

I used the drug on a series of over fifty consecutive operations on the globe of the eye, most of them for cataract, some for acute and chronic glaucoma. The strengths of the various solutions employed were as follows: viz, a 1 in 200 solution for superficial anaesthesia by instillation into the conjunctival sac, a 1 in 500 solution for akinesia of the orbicularis oculi by blocking the seventh cranial nerve, and a 1 in 250 solution for anaesthesia of the iris by blocking the ciliary nerves. A few enucleations also were performed under local anaesthesia with this drug. The anaesthesia and akinesia were perfect in every way in all the cases. This drug does not seem to exert such an amount of desiccating effect on the corneal epithelium as does cocaine.

The list price of the drug is Rs. 2 per gramme, the cost of the same quantity of cocaine being Rs. 1-8. But considering that this drug is used in one-tenth of the strength of cocaine, it is, thus, really many times cheaper than cocaine. Compared with novocaine and ethocain also, it is cheaper for local anaesthesia, as for this purpose too it is used in one-tenth of the strength in which these drugs are used.

In the matter of resisting the effects of repeated sterilization, I had a striking demonstration of the advantage this drug has over cocaine. About two drachms of the solution were left after use and this happened to be sterilized day after day for over six weeks, the bottle having been left in the sterilisable set with other solutions. Subsequently, the solution was used on two cases for instillation and anaesthesia was perfect.

The solution can be prepared in plain distilled water but the makers recommend physiological saline as the solvent. I have found that the latter is more satisfactory. If there is any trace of alkali in the solvent, the solution of Pantocain becomes slightly cloudy, but this in no way interferes with the action of the drug. This drug is entirely free from the toxic effects of cocaine and is a very safe one to use.

Taking into consideration its cheapness, freedom from toxicity and absence of dehydrating effect on the cornea, I am of opinion that this drug can very well replace cocaine, and novocain or ethocain almost, if not quite, completely in ophthalmic practice.

Yours, etc.,

C. V. KRISHNASWAMI,

CAPTAIN, A.I.R.O.

M.B., B.S. (Mad.), D.O.M.S. (Lond.), F.R.C.S.E.,

Honorary Ophthalmic Surgeon.

GOVERNMENT HEADQUARTER HOSPITAL,
MADURA,

14th December, 1932.

Service Notes

APPOINTMENTS AND TRANSFERS

BREVET-COLONEL G. D. FRANKLIN, C.I.E., O.B.E., K.I.S., on return from leave, resumed charge of the duties of the Residency Surgeon, Hyderabad, with effect from the forenoon of the 9th December, 1932.

Lieutenant-Colonel A. D. Stewart was appointed temporarily as Director, All-India Institute of Hygiene and Public Health, Calcutta, with effect from the 1st January, 1932, and is confirmed in that appointment, with effect from the 23rd December, 1932.

Lieutenant-Colonel A. J. H. Russell, C.B.E., is appointed to officiate as Deputy Director-General, Indian Medical Service, with effect from the 1st January, 1933.

The services of Lieutenant-Colonel E. S. Goss, M.C., officiating Deputy Director-General, Indian Medical Service, are placed at the disposal of the Army Department, with effect from the 1st January, 1933.

Major J. Rodger, M.C., an Agency Surgeon, on return from leave, is posted as Civil Surgeon, Sibi, with effect from the forenoon of the 20th October, 1932. (The previous notification dated 10th November, 1932, on the subject is hereby cancelled.)

The services of Major P. A. Dargan are placed permanently at the disposal of the Government of the Punjab, with effect from the 17th April, 1931.

The services of Major G. H. Fraser are placed at the disposal of the Government of Burma for appointment as Superintendent, Mental Hospital, Tadagale, Rangoon, with effect from the 31st December, 1932.

The services of Captain H. S. Waters are placed temporarily at the disposal of the Government of Bombay, with effect from the forenoon of the 5th December, 1932.

Captain E. A. Y. Mackcown is appointed to officiate as ex Officer, Saugar Cantonment, in addition to his ordinary duties, *vice* Captain A. S. Sullivan, M.C. Dated 2nd December, 1932.

RETIREMENTS

Colonel W. R. J. Scroggie, C.I.E. Dated 23rd January, 1933.

Lieutenant H. Hannesson relinquishes his probationary appointment, 30th November, 1932.

Notes

THE ANNALS OF THE TOMARKIN FOUNDATION

The *Annals* of the Tomarkin Foundation, which is an international institution run very much on the lines of the Rockefeller Foundation, only on a smaller scale, are published quarterly. The range of subjects of the papers that are published in these *Annals* is a comprehensive one, but the majority of the papers report investigations that have a very practical application in the treatment and diagnosis of disease. Most of the papers in the number we have received are written in German, but a few are in French. Contributions from a number of well-known workers are included; for example there is a paper by Besredka on local vaccine therapy in intestinal infections, one by Calmette on the filterable elements in the virus of tuberculosis, one by Sachs on the problems of serum diagnosis, and one by Hauns Alexander on the work therapy in lung conditions.

The *Annals* are well printed on a good quality of paper, and should be in every comprehensive medical library.

The price of the publication is M. 16 annually, and the publisher is Georg Thieme, Leipzig.

MYCOZOL

Mycozol ointment contains chlorctone (chlorbutanol) 5 per cent., salicylic acid 4 per cent. and mercury salicylate 4 per cent., together with aromatics. The method utilized in its manufacture, and the nature of the base, results in a smooth, adhesive ointment that is rapidly absorbed by the skin, bringing the active ingredients into intimate contact with the deeper layers and preventing saturation of the dressings.

Mycozol is an effective remedial agent for the treatment of a number of skin lesions, classed under the general term 'epidermomycosis' and commonly referred to as 'foot itch', 'athletes' foot itch', 'swimmers' itch', 'jockey-strap itch', 'dhubie itch', and 'ringworm of feet'.

It is estimated that 50 to 75 per cent. of adults have some degree of fungus affection, particularly of the hands, feet, groin, axillæ, breast. In tropical countries this percentage is much higher; it would be no exaggeration to place it at 90 per cent.

It is generally agreed that in the treatment of epidermomycosis the best results are produced when a keratolytic, anti-pruritic and anti-parasitic ointment is chosen. With this in mind, Mycozol was developed, and successful clinical application warrants its extended use in all skin affections caused by the genus epidermophyton. Mycozol is non-irritating. It produces rapid maceration and the separation or peeling of the horny layers of the epidermis (Keratolysis), thus exposing the fungi to its inhibitive, possibly curative, action.

Mycozol is used to best advantage in the following manner, especially in the treatment of epidermophytosis of the hands and feet. This routine is modified somewhat in handling lesions in the region of the groin and the axillæ.

Scrub the affected area with a small, soft-bristled brush, using warm water and a thick lather of some germicidal soap (e.g., Neko 1 per cent.) or tincture of green soap. A soft tooth brush is suitable for the purpose.

After scrubbing, dry the parts with a soft cloth.

Apply alcohol and allow this to evaporate in the air until the parts are dry.

Mycozol is thoroughly rubbed into the affected parts, and a liberal excess allowed to remain on the skin; the area is then covered with cotton or gauze, held in place by a bandage and left on overnight.

The Mycozol is removed in the morning by means of talcum powder, before bathing.

Repeat the procedure each night until desquamation is complete and no more bullae, vesicles, papules or macules are observed.

Caution.—In dressing the affected areas, as small an amount of Mycozol as possible should be allowed to come in contact with the normal skin; and in any location where chafing might result from attrition of opposing surfaces, if Mycozol is required, it should be applied sparingly.

Packages.—Mycozol is supplied in one-ounce tubes, each tube provided with a label that can be slipped off for convenience in prescribing. The tubes are marketed in individual cartons, twelve to the package.

ELECTRO-MEDICAL APPARATUS

WATSON & SONS (Electro-Medical) are known throughout the world as manufacturers of high-class electro-medical apparatus. Their latest catalogue shows a very wide range of modern apparatus for use in almost all special branches of medical science. The appliances in which they specialize are diathermy and cautery apparatus. It is difficult to make a selection for special mention, but the 'Sunic' junior diathermy apparatus has many features which should appeal to the medical man in this country; the price complete is £55, where an alternating current is available. The makers claim that it is an instrument of robust construction and of reliability in performance. The spark gap is of a special type with large contacts, so that the output is smooth and the machine is capable of continuous work. Other special features which they claim are:—

1. New type cabinet, white enamel with glass top.
2. Vertical mounting of controls—conveniently manipulated.
3. All parts easily accessible.
4. Vacuum impregnated mica condenser in porcelain case.
5. Potentiometer control giving smooth variation of output, zero maximum.
6. Thermo-couple ammeter.
7. Smooth output as follows:—

Load resistance	Current	Watts (I ² R)
25 ohms.	2.9 amps.	210
50 "	2.1 "	220
100 "	1.45 "	210
200 "	1.0 "	200
8. Short circuit current of the order of 6 ampères.
9. Improved 'Sunic' spark gap with 9/16 inch diameter contacts—two contacts, four points.

Their infra-red lamp is one that should be useful to practitioners, and again the price is moderate. This lamp consists of a special high-power evacuated bulb, giving a powerful output of infra-red rays. It can be used singly for infra-red therapy or in conjunction with the mercury vapour lamp.

The bulb is mounted in a double-walled reflector, 18 inches in diameter, designed to give ample ventilation. A wattage of 1,500 can be employed without undue risk of damage to the bulb. The reflector is hung on a wall bracket with counterweight arrangement, which allows of ample movement in all directions. A red glass screen, made in strips to avoid breakage due to expansion, can be fitted to the hood.

The firm's office in India is at Commercial House, Currimbhoy Road, Ballard Estate, Bombay, and the head office is Sunic House, Parker Street, Kingsway, London, W.C.2.

RADIOGRAPHIC EXAMINATION OF THE GALL-BLADDER

For the radiographic examination of the gall-bladder there are two useful products, 'Stipolae' brand tetra-iodophenolphthalein and 'Wellcome' brand sodium

tetra-iodophenolphthalein. The 'Stipolae' brand tetra-iodophenolphthalein product is supplied in two tubes containing 'Stipolae' sodium tetra-iodophenolphthalein and 'Stipolae' acid mixture, respectively. 'Wellcome' brand sodium tetra-iodophenolphthalein is intended for use in intravenous administration.

Administration

The patient is given a 'mild' aperient—preferably castor oil—24 hours before the product is administered. A light meal (nothing at all afterwards) is taken at 6 P.M. on the following day, and at 9 P.M. the whole contents of the two tubes containing 'Stipolae' sodium tetra-iodophenolphthalein and 'Stipolae' acid mixture, prepared as directed, are given. Radiograms are taken at 9-30 A.M. and 12-30 P.M. next day. If a good shadow is obtained, a meal rich in fat, e.g., egg-yolks, which hastens the emptying of the gall-bladder, is given, and a third radiogram is taken at 3-30 P.M. If this radiogram shows the gall-bladder to be empty or nearly so, i.e., the shadow reduced in size, the gall-bladder is probably normal. If it has not emptied, or the shadow is very indistinct, further investigation of the patient is necessary. In a normal gall-bladder, a shadow is visible 12 hours after administration of the dye; after 15 hours it is denser and usually smaller; two to three hours after the meal of fat, the shadow should be absent or much reduced.

These products are issued by Burroughs Wellcome & Co., of Snow Hill Buildings, London, E.C.1, and Cook's Building, Hornby Road, Bombay.

TYCOS SCIENTIFIC INSTRUMENTS

THE writings of the early philosophers responsible for experiments which ultimately led to discoveries resulting in the birth of the barometer include those of Anaxagoras (500 to 428 B.C.), Empedocles (504 to 443 B.C.), the more definite ideas of Aristotle (385 to 322 B.C.), and the concepts of Seneca (54 B.C. to 39 A.D.), the last-named being very familiar with the 'Meteorologica' of Aristotle.

After about the first century the prosecution of science ceased, and it was not until the era of Galileo, A.D. 1613, that anything definite is recorded as to further progress. He commended to his pupil, Torricelli (A.D. 1645), that his experiments be continued, but Torricelli died before the discovery was fully completed.

Pascall (A.D. 1648) discovered that atmospheric pressure varied at different elevations, and thus demonstrated the theory of altitude measurements. It was not until A.D. 1665 that the barometer received its name, when an unsigned note (attributed by some to Robert Boyle), appeared in the *Philosophical Transactions* referring to a 'new kind of barometer which may be called statical'.

Dr. Hooke (A.D. 1686) produced the first type of mercurial weather barometer of the 'wheel type'.

Conté (A.D. 1798) was responsible for the first metal barometer known as the 'Aneroid', derived from the Greek words meaning 'without fluid'.

Vidi (A.D. 1841) improved on the aneroid of Conté by designing an aneroid barometer with a corrugated vacuum box which gave a greater elasticity to the movement.

Sir G. B. Airy, K.C.B. (A.D. 1801 to 1881) compiled a scale of feet measurements to match the scale of inches of pressure on the barometer.

Admiral Fitzroy, R.N., F.R.S. (A.D. 1805 to 1865), was responsible for weather indications known to-day as 'Fitzroy words'.

This note is extracted from the catalogue of Short and Mason, Ltd. They are manufacturers of a very big range of meteorological and other scientific instruments; their Tycos 'Stormographs' are extensively used in this country. This catalogue contains descriptions of a number of instruments suitable for both domestic and scientific use. Their thermo-hygrometers are of a pattern which will appeal to the malariologist and the research worker.

The head office and factory of the firm are the Aneroid Works, Walthamstow, London, E.17, and their local agents are, L. H. Alliston & Co., Ltd., Clive Buildings, Calcutta.

NEOSALVARSAN

It has been brought to our notice that a small chemist firm in the Punjab is keeping and offering for sale a consignment of Neosalvarsan, which was not imported through our firm, the only legal channel for India, Burma and Ceylon. The packings bear French labels and do not show the usual batch-control number in four Roman capitals (e.g., VXL M, etc.) which, in the legally imported stocks, is always shown on the left hand side of the attached label on the packing box as well as on the label of the ampoule itself. Further, the packings from this consignment also do not possess the protective labels with the name of our firm.

The sample ampoule, which was sent to us, shows on the bottom of the packing box the number A-33925. From this we have been able to find out that the consignment left the factory of our manufacturers on the 12th December, 1912 (i.e., 20 years ago), and was sold to a customer in Constantinople. The content of the ampoule was found to give a very turbid solution of rather reddish tint, indicating thereby its absolute unfitness for use. It is not known to us how many ampoules of the contraband consignment are now being actually offered for sale; nor can we assert if all the packings thereof bear the same number, viz., A-33925.

However, we strongly warn the medical profession against accepting and using such contraband packings of Neosalvarsan. We should like to remind them once again that all genuine and legally imported packings of Neosalvarsan do invariably bear the batch-control number in Roman capitals, and are further guaranteed by the protective label round the packing having the well-known inscription:

'Specially manufactured for the tropics and packed for British India and Ceylon. Imported by Messrs. Havero Trading Co., Ltd., Calcutta, Bombay and Madras.'

Under the circumstances, we beg to declare that no responsibility or obligation whatever may be expected from our side, should any mishap occur by and through the use of such contraband packings of Neosalvarsan.

'Bayer-Meister Lucius,'
Havero Trading Co., Ltd.,

Pharmaceutical Dept.,
15, Clive Street,

P. O. Box 2122,
Calcutta.

ANTIPHLOGISTINE SUBSTITUTES

THE following notice has been sent to us by the manufacturers of Antiphlogistine:—

When a physician prescribes a product which his experience and skill has demonstrated to be the best treatment for some special condition, he has a right to that product—moreover, his patient is entitled to that product. Anything less than this will not suffice! Not only is substitution of a medical product, immoral, but the manufacturer or retailer who encourages the use of his own or other imitations is not only jeopardizing his reputation and standing, but is betraying the confidence of his clients.

Many cases are on record where substitutions made to look and smell like Antiphlogistine have caused much suffering, and instances are not rare where the actual life of the patient has been sacrificed through the use of inert and even dangerous substitutes.

Antiphlogistine, a scientific therapeutic remedy, is compounded to bring relief to suffering humanity—imitators deceive the suffering for a profit, often jeopardizing the health and life of those who are unable to recognize the fraud. Physicians should warn their patients and clients of the inert, harmful and dangerous substitutes which are now flooding India to be sold in place of the genuine Antiphlogistine.

Antiphlogistine cannot be successfully imitated—the process and laboratory apparatus for compounding, and the peculiar silicate of aluminium base obtained from privately-owned mines are available to none other than the Denver Chemical Manufacturing Company.

'SCIATAGO'

UNDER the above name, Messrs. Coates & Cooper, Ltd., 94, Clerkenwell Road, London, E.C. 1, have issued a preparation in dragées, stated to consist of phenol-quinolin-carboxylic acid, hexamethylene-tetramine, and glyccoll, a formula which has been used with success for some time on the Continent in the treatment of rheumatism, sciatica, and lumbago. The preparation is put up in tins each containing 40 dragées of 3 grammes each, the dose being two dragées twice daily after a light meal. Treatment should be continued for 2 to 3 weeks, and a second course may be prescribed after an interval of 2 weeks. The firm will be glad to send samples and literature upon request by members of the medical profession.

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Original Articles

AN ANALYSIS OF ONE HUNDRED AND FIFTY CASES OF ASTHMA

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THIS investigation was undertaken in order to find out the cause of the syndrome of asthma in each individual case so that a rational treatment could be given to each patient. In all, one hundred and sixty-one cases were investigated, of these only one hundred and fifty were included in the analysis; eleven cases were rejected as they were found to be cases of chronic bronchitis alone. The investigation included physical examination of the patient, blood examination as regards the total leucocytes, total eosinophiles and Arneth's count, smear and cultural examinations of the sputum, as well as examinations of the stools for *Entamoeba histolytica*, ova of helminths and pathogenic bacteria. Dermal tests were done with extracts made from the hairs and feathers of common animals and from common foods. Usually a von Pirquet's test was done and a skiagram was taken of the chest. Where indicated, expert advice was obtained on the state of the nose, throat and para-nasal sinuses.

Clinically the cases could be divided into three groups:—

(1) Cases due to chronic bronchitis, bronchiectasis and other chronic lesions of the lung. In these cases there was no evidence of allergy, and the age of onset of the disease was usually above twenty years (in 50 per cent. of the cases above thirty years). This group included seventy-nine of our cases, i.e., about 53 per cent. of all the cases.

(2) Bronchial cases in which Gram-negative bacilli were present in smears made from the sputum and were also isolated from the sputum in cultures. This group formed a clinical entity because of the presence of these bacilli and the associated high blood eosinophilia in contrast to the usually low blood eosinophilia in group (1). This group includes twenty-seven of our cases, i.e., 18 per cent. of the total cases. These cases have been described by us in a separate paper.

(3) This group contains three types of case. Firstly, cases due to some external allergen, secondly, cases due to some allergen from the gut, and, thirdly, those bronchial cases which were not definitely allergic but in which there was some evidence of allergy in the shape of

heredity, early age of onset, or positive dermal tests. For purposes of simplification we have included all these three types in one group which we have called the allergic group. This group includes forty-four cases, i.e., about 30 per cent. of the total cases. The distribution of these allergic cases amongst Indians and Europeans is rather interesting and will be referred to later in this paper.

THE ANALYSIS.

(1) *The total leucocytes, the number of polymorphonuclears and eosinophiles per cubic millimetre of blood.*—The total leucocyte and eosinophile counts are important from the diagnostic point of view. This question has been discussed by us in a separate paper. The Gram-negative-bacilli cases and the allergic cases show a high blood eosinophilia in contrast to the usually low figures in bronchial cases. No information of any value was obtained from the polymorphonuclear count.

(2) *The Arneth's count which is of great help in differentiating the bronchial cases from the allergic.*—In the bronchial and Gram-negative-bacilli cases there is usually a marked shift to the left, in true allergic cases the count is more or less unaffected, but in bronchial cases showing some evidences of allergy there is also a marked shift to the left. If we express the Arneth's count in terms of Arneth's index (the sum of the first two columns plus half of the third column) we find that:—

(a) In sixty-nine out of seventy-nine bronchial cases, the Arneth's index was above seventy.

(b) In nineteen of twenty-seven Gram-negative-bacilli cases, the Arneth's index was above seventy.

(c) In twenty out of thirty-seven allergic cases the Arneth's index was below seventy; only in seventeen cases it was above seventy and these seventeen cases were bronchial cases with allergy.

(3) *The total eosinophile count and Arneth's count considered together.*—We find that:—

(i) A low eosinophile count with a marked shift in Arneth's count to the left is usually found in bronchial cases.

(ii) A low eosinophile count with little or no shift in Arneth's count is found in some allergic cases (without high eosinophilia).

(iii) A high eosinophile count with a marked shift in the Arneth's count to the left is found in the Gram-negative-bacilli cases, in the mixed type of bronchial and allergic, and in some bronchial cases having a high eosinophilia.

(iv) A high eosinophile count with little or no shift in Arneth's count is usually found in allergic cases.

(4) *Heredity.*—Forty cases gave a history of inheritance. A history of heredity is more common in the Gram-negative-bacilli cases than in the other types. There is no correlation between heredity and blood eosinophilia, sputum

eosinophilia, or age of onset of the disease as is shown in table I. eosinophiles varied from a small percentage of the cellular exudate to nearly all the cells being

TABLE I

	Total number of cases	Cases giving history of inheritance	Blood eosinophilia in cases showing heredity	Sputum eosinophilia in cases showing heredity	Age of onset in cases showing heredity
Bronchial cases	79	15	3 cases eosinophiles under 250 per c.mm. 4 cases eosinophiles between 250 and 500 per c.mm. 3 cases eosinophiles between 500 and 750 per c.mm. 3 cases eosinophiles between 750 and 1,000 per c.mm. 2 cases eosinophiles above 1,000 per c.mm.	11 cases no eosinophiles in sputum. 1 case majority of the cells eosinophiles. 2 cases a few eosinophiles. 1 case there was no sputum.	2 cases started in childhood. 1 case started between 5 and 10 years. 1 case started between 11 and 15 years. 1 case started between 16 and 20 years. 4 cases started between 21 and 30 years. 6 cases started above 30 years.
Gram-negative-bacilli cases.	27	13	1 case eosinophiles under 750 per c.mm. 3 cases eosinophiles between 750 and 1,000 per c.mm. 9 cases eosinophiles ranging from 2,000 to 11,000 per c.mm.	8 cases no eosinophiles in sputum. 5 cases eosinophiles in sputum.	2 cases started between 11 and 15 years. 2 cases started between 16 and 20 years. 6 cases started between 21 and 30 years. 3 cases started above 30 years.
Allergic cases	44	12	2 cases eosinophiles under 250 per c.mm. 2 cases between 250 and 500 per c.mm. 2 cases eosinophiles between 500 and 1,000 per c.mm. 2 cases eosinophiles under 3,000 per c.mm. 2 cases eosinophiles under 4,000 per c.mm. 2 cases eosinophiles under 9,000 per c.mm.	5 cases no eosinophiles in sputum. 4 cases eosinophiles in sputum. 3 cases no sputum.	5 cases started in childhood. 1 case started between 5 and 10 years. 1 case started between 11 and 15 years. 1 case started between 16 and 20 years. 2 cases started between 21 and 30 years. 2 cases started above 30 years.
TOTAL	150	40	5 cases under 250 per c.mm. 6 cases between 250 and 500 per c.mm. 5 cases between 500 and 750 per c.mm. 7 cases between 750 and 1,000 per c.mm. 17 cases above 1,000 per c.mm.	24 cases no eosinophiles in sputum. 12 cases eosinophiles in sputum. 4 cases no sputum.	7 cases started in childhood. 2 cases started between 5 and 10 years. 4 cases started between 11 and 15 years. 4 cases started between 16 and 20 years. 12 cases started between 21 and 30 years. 11 cases started above 30 years.

(5) *Sputum eosinophilia*.—Thirty-six cases had eosinophiles in the sputum, the number of eosinophiles. Table II shows the incidence of sputum eosinophilia amongst the three groups.

TABLE II

	Total number of cases	Cases showing eosinophiles in sputum	Blood eosinophilia in cases showing sputum eosinophilia	Heredity in cases showing sputum eosinophilia
Bronchial cases ..	79	16	5 cases eosinophiles below 250 per c.mm. 6 cases eosinophiles between 250 and 500 per c.mm. 1 case eosinophiles under 2,000 per c.mm. 1 case eosinophiles under 4,000 per c.mm.	Only 3 cases show heredity.
Gram-negative-bacilli cases.	27	8	1 case eosinophiles under 750 per c.mm. 1 case eosinophiles under 1,000 per c.mm. 1 case eosinophiles under 3,000 per c.mm. 1 case eosinophiles under 5,000 per c.mm. 1 case eosinophiles under 6,000 per c.mm. 1 case eosinophiles under 7,000 per c.mm. 1 case eosinophiles under 10,000 per c.mm. 1 case eosinophiles under 11,000 per c.mm.	Only 5 cases show heredity.
Allergic cases ..	44	12	2 cases eosinophiles under 500 per c.mm. 2 cases eosinophiles under 750 per c.mm. 1 case eosinophiles under 1,000 per c.mm. 2 cases eosinophiles under 2,000 per c.mm. 1 case eosinophiles under 3,000 per c.mm. 1 case eosinophiles under 6,000 per c.mm. 1 case eosinophiles under 7,000 per c.mm. 2 cases eosinophiles under 12,000 per c.mm.	Only 4 cases show heredity.
TOTAL ..	150	36	5 cases eosinophiles under 250 per c.mm. 8 cases eosinophiles between 250 and 500 per c.mm. 3 cases eosinophiles under 750 per c.mm. 5 cases eosinophiles under 1,000 per c.mm. 3 cases eosinophiles under 2,000 per c.mm. 2 cases eosinophiles under 3,000 per c.mm. 10 cases eosinophiles above 3,000 per c.mm.	Only 13 cases show heredity.

TABLE III

	Total number of cases	NUMBER OF CASES STARTING					
		in infancy and childhood	between 5 and 10 years of age	between 11 and 15 years of age	between 16 and 20 years of age	between 21 and 30 years of age	after 30 years of age
Bronchial cases ..	79 Age of onset not known in 1 case.	3 (H in 2)	4 (H in 1)	3 (H in 1)	3 (H in 1)	27 (H in 4)	38 (H in 6)
Gram-negative-bacilli cases.	27	4 (H in 2)	6 (H in 2)	12 (H in 6)	5 (H in 3)
Allergic cases ..	44 Ages of onset not known in 6 cases.	12 (H in 5)	2 (H in 1)	4 (H in 1)	4 (H in 1)	7 (H in 2)	9 (H in 2)
TOTAL ..	150 Ages of onset not known in 7 cases.	15 (H in 7)	6 (H in 2)	11 (H in 4)	13 (H in 4)	46 (H in 12)	52 (H in 11)

H = history of inheritance.

The table also shows that there is no correlation between the sputum eosinophilia and blood eosinophilia or between sputum eosinophilia and heredity.

(6) *Age of onset of the disease.*—Table III shows the ages of onset in the three groups of

(8) *Von Pirquet's test.*—This was performed in ninety-three cases with forty-seven negative and forty-six positive results. Table V shows these results. It will be noted that the test was positive in more than half of the bronchial cases tested, both the bronchial and Gram-

TABLE IV

	Total number of cases	Number of cases in which dermal tests were done	RESULTS		Positive	Particulars of positive tests
			Negative	Doubtful		
Bronchial cases	79	67	57	3	7	4 cases positive to bacterial extracts. 3 of these cases eosinophiles under 500 per c.mm. 1 of these cases eosinophiles under 6,000 per c.mm. 1 case positive to grass pollens. Eosinophiles 750 per c.mm. 1 case positive to horse-hair. Eosinophiles 750 per c.mm. 1 case positive to cattle-hair. Eosinophiles 3,000 per c.mm.
Gram-negative-bacilli cases.	27	25	22	..	3	1 case positive to cattle-hair. Eosinophiles 10,000 per c.mm. 1 case positive to grass pollens. Eosinophiles 5,000 per c.mm. 1 case positive to foods. Eosinophiles 6,000 per c.mm.
Allergic cases	44	41	14	9	18	8 cases positive to different foods. 10 cases positive to feathers, hairs, dust, etc. In half of the cases the blood eosinophiles were below 1,500 per c.mm., while in the other half they were above this figure.
TOTAL ..	150	133	93	12	28	

cases. It will be seen that the majority of the bronchial cases start after twenty years of age, the Gram-negative-bacilli cases start rather earlier, and most of the allergic cases start very early; eighteen out of thirty-eight started before fifteen years of age. The table also shows that there is not much correlation between heredity and the age of onset.

(7) *Dermal tests.*—The results of the dermal tests are shown in table IV. It is evident from the table that in the bronchial and Gram-negative-bacilli cases the dermal tests are of no value. In allergic cases, where the trouble is due to emanations from hair, feathers or dust, these tests are of value, but in allergic cases dependant on some pathological condition of the gut the dermal tests are valueless. The tests are either all negative or all positive. The table also shows that there is some correlation between positive dermal tests and the high blood eosinophilia in bronchial and Gram-negative-bacilli cases.

negative groups, and in only 4 out of 17 allergic cases.

(9) *Evidence of tuberculosis.*—Clinical or radiological evidence of pulmonary tuberculosis was found in eighteen cases, fifteen of these were included in the bronchial group and three in the Gram-negative-bacilli group. Table VI shows the distribution of these cases and their relation with the Von Pirquet test and blood eosinophilia.

(10) Only in one case there was some other co-existing allergic manifestation present (allergic dermatitis).

(11) Amongst the allergic group there were four cases in which the attacks of asthma were associated with the locality, the patients being free from attacks when they kept away from that particular place. No such association was seen amongst the bronchial or Gram-negative-bacilli cases.

(12) In three cases some special food was responsible for the attacks or made the attack worse.

(13) There were twenty-two females in this

pneumonia and chronic bronchitis. A history of previous pneumonia was more common in the Gram-negative-bacilli cases than in bronchial cases; it was much less common in allergic

TABLE V

	Total number of cases	Number of cases in which Von Pirquet's test was done	RESULTS	
			Negative	Positive
Bronchial cases	79	60	25	35
Gram-negative-bacilli cases ..	27	16	9	7
Allergic cases	44	17	13	4
TOTAL	150	93	47	46

TABLE VI

	Total number of cases	NUMBER OF CASES SHOWING EVIDENCE OF TUBERCULOSIS				Result of Von Pirquet's test in tuberculous cases	Blood eosinophiles in tuberculous cases
		Early	Advanced	Old healed	Total		
Bronchial cases	79	1	4	10	15	Von Pirquet positive in 13 cases. Von Pirquet negative in 2 cases of old healed lesions.	5 cases eosinophiles below 250 per c.mm. 5 cases eosinophiles between 250 and 500 per c.mm. 1 case eosinophiles between 500 and 750 per c.mm. 2 cases eosinophiles between 750 and 1,000 per c.mm. 2 cases eosinophiles above 1,000 per c.mm.
Gram-negative-bacilli cases.	27	3	3	Von Pirquet positive in 1 case. Von Pirquet negative in 2 cases.	1 case eosinophiles under 1,000 per c.mm. 1 case eosinophiles under 2,000 per c.mm. 1 case eosinophiles under 6,000 per c.mm.
Allergic cases	44
TOTAL ..	150	1	4	13	18	Von Pirquet positive in 14 cases. Von Pirquet negative in 4 cases.	14 cases eosinophiles under 1,000 per c.mm. 4 cases above 1,000 per c.mm.

series and of these two gave a history of association of the attacks with the menstrual periods.

(14) *Pre-asthmatic state*.—Seventy-one patients gave a history of having suffered from

cases. On the other hand, a history of previous dysentery was more common in allergic cases than in the bronchial and Gram-negative-bacilli cases. Table VII gives a résumé of the pre-asthmatic states.

(15) The relation of weather and seasons to the condition of the patients is shown in negative-bacilli cases usually showed enlarged hilus shadows and a good deal of fibrosis

TABLE VII

	Total number of cases	Number of cases showing previous illness	Pneumonia	Chronic bronchitis	Nose and throat troubles	Dysentery	Urticaria
Bronchial cases	79	52	16	30	4	1 (6 cases put under chronic bronchitis had suffered from dysentery.)	1 (4 cases under pneumonia and chronic bronchitis had suffered from urticaria.)
Gram-negative-bacilli cases.	27	18	8	7	2	1 (3 cases under pneumonia and bronchitis had suffered from dysentery.)	(2 cases under pneumonia had suffered from urticaria.)
Allergic cases	44	21	5	5	3	7 (1 case under pneumonia had suffered from dysentery.)	1 (3 cases under pneumonia had suffered from urticaria.)
TOTAL ..	150	91	29	42	9	9 (10 cases under bronchitis and pneumonia had suffered from dysentery.)	2 (9 cases under bronchitis and pneumonia had suffered from urticaria.)

table VIII; bronchial cases are most affected by the change of seasons and the allergic cases the least.

(figure 2). Three cases amongst the Gram-negative-bacilli group showed calcified Assmann's foci—tuberculous lesions under the

TABLE VIII

	Total number of cases	Number of cases showing seasonal variation	Cases which are worse in winter or rains, or in which attacks only occur in these seasons	Cases which are worse in summer	Cases which are worse in extremes of temperature (heat and cold)
Bronchial cases ..	79	35	29	3	3
Gram-negative-bacilli cases.	27	10	7	1	2
Allergic cases ..	44	16	12*	1	3
TOTAL ..	150	61	48	5	8

* These cases are mostly bronchial cases with some evidence of allergy.

(16) The ether test for proteoses was done in seventy-five cases with sixty-eight positive and seven negative results, as shown in table IX.

(17) Skiagram of the chest.—In the allergic cases the x-ray picture was as a rule quite normal (figure 1). The bronchial and Gram-

clavicle (figures 3 and 4). Amongst the bronchial cases apart from the healed lesions evidence of active disease was found in five cases; out of these there was an early lesion in one case (figure 5) and well advanced lesions in four cases (figures 6, 7 and 8).

PLATE III

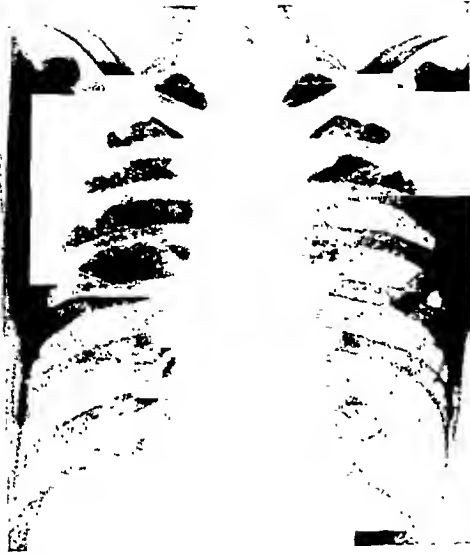


Fig. 1.—Skiagram from a case secondary to gut infection. The lungs are quite normal.

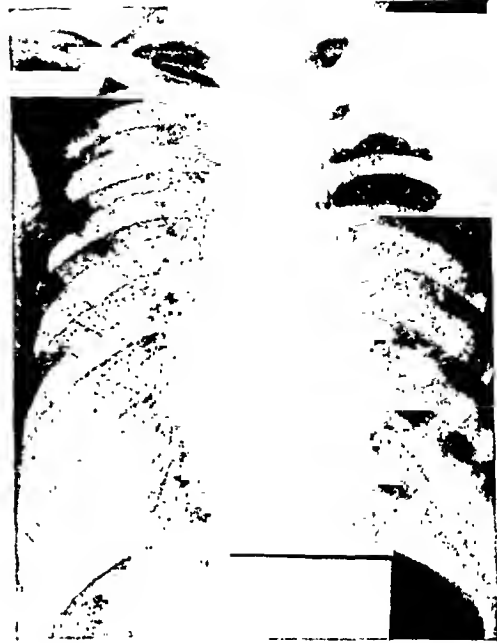


Fig. 2.—Skiagram from a bronchial case. Increased fibrosis and enlarged hilus glands.

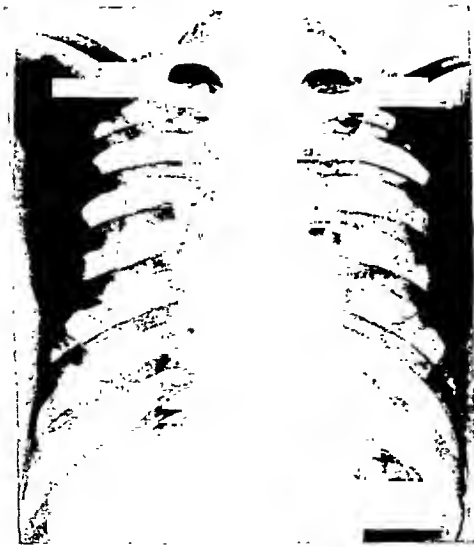


Fig. 3.—Skiagram from a bronchial case. A calcified focus in the right upper lobe.

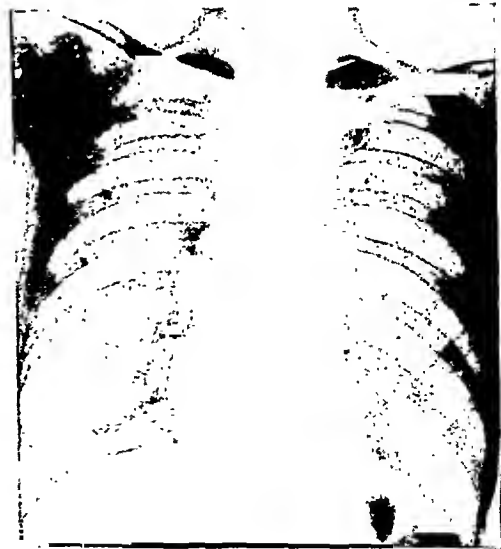


Fig. 4.—Skiagram from a bronchial case. Two calcified areas in the left upper lobe.

PLATE IV

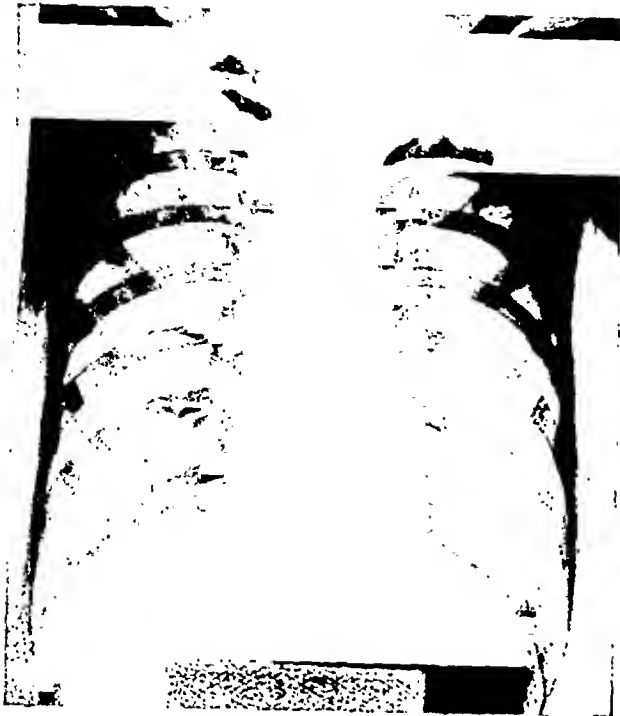


Fig. 5.—Early tuberculous focus in right lung $\frac{1}{4}$ inch below the apex.

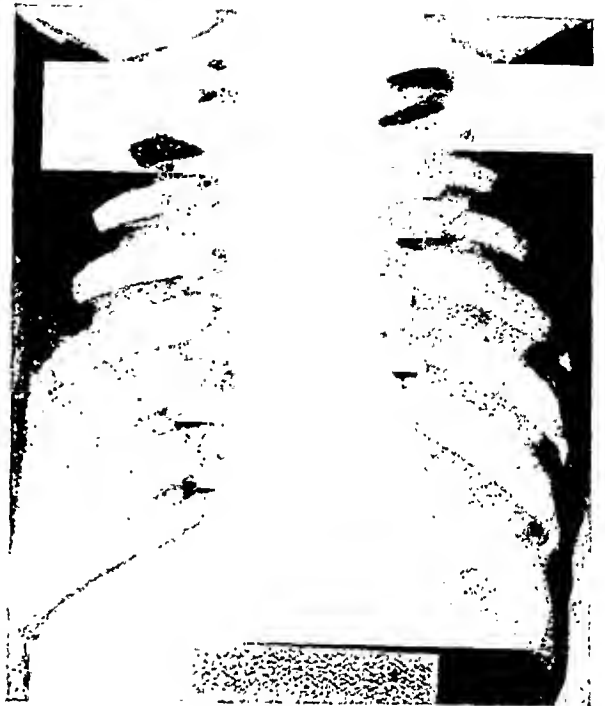


Fig. 6.—Right apex extensively infiltrated.

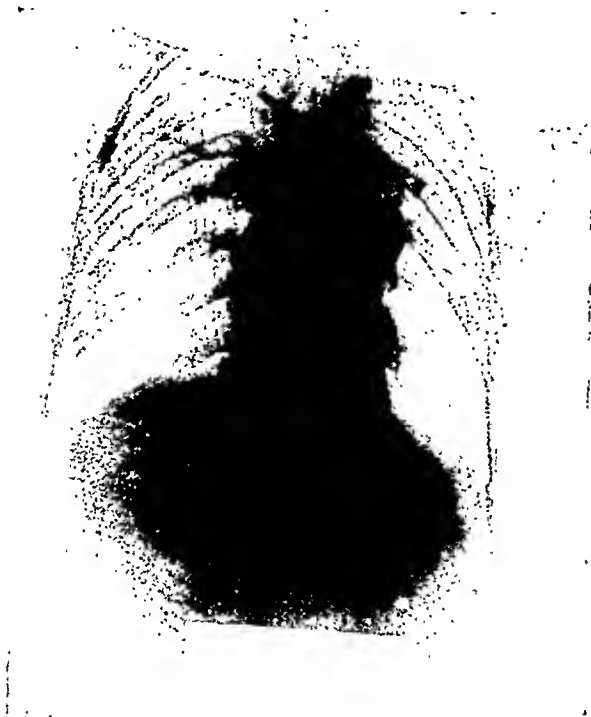


Fig. 7.—Extensive lesion of right upper and middle lobes with extension into lower lobe. Early disease left side, lower part of upper lobe.



Fig. 8.—Complete consolidation of left upper lobe.

(18) *Therapeutic test.*—Attacks in most of the bronchial cases were controlled by A. P. C. powders (aspirin grs. v, phenacetin grs. iii, and caffeine grs. iii), some of the cases required injections of morphia. The Gram-negative-bacilli cases responded both to A. P. C. and adrenalin injections, the adrenalin being on the whole more useful. The allergic cases did well with adrenalin injections.

European cases 13 out of 35 and on the Indian side only 31 were diagnosed as due to allergy.

(ii) Out of the thirteen cases of allergy in Europeans ten were due to external excitants and three to gut infections; amongst the Indians out of thirty-one cases only twelve were due to external excitants and nineteen to gut infections. So that the European cases are more sensitive to external allergens than the Indian

TABLE IX

	Number of cases in which the ether test for proteoses was done	Result positive	Result negative
Bronehial cases	44	40	4
Gram-negative-bacilli cases	19	17	2
Allergic cases	12	11	1
TOTAL	75	68	7

TABLE X

	Total number of cases	Total number of cases showing allergy	CASES SHOWING ALLERGY		Evidences of allergy in cases probably due to external excitants
			Number of cases in which the allergy is due to gut conditions	Number of cases in which the allergy is due to external excitants	
Europeans	35	13	3	10	3 cases. Positive dermal tests—association with the excitant brings on attack. 1 case. Heredity—positive dermal tests—onset at early age. 2 cases. Positive dermal tests. 2 cases. Onset at early age (3 and 6 years)—doubtful dermal tests. 1 case. Starting in infancy. 1 case. Heredity—onset at comparatively early age.
Indians ..	115	31	19	12	1 case. Positive dermal test—association with excitants brings on attack—the patient successfully desensitised with repeated small doses of the excitant. 4 cases. Heredity—asthma at early age. 2 cases. Asthma starting at early age. 1 case. Heredity—positive dermal tests. 3 cases. Positive dermal tests. 1 case. Doubtful dermal tests.

(19) *Allergic cases.*—The distribution of allergic cases amongst Indians and Europeans is rather interesting and is put down in the above table.

A perusal of the above table brings out the following points.

(i) Allergic cases are more common amongst Europeans than amongst Indians; of the

cases amongst whom only 10 per cent. are sensitive to external allergens. On the other hand few of the Europeans were sensitive to allergens from the gut whilst 19 out of the 31 Indian allergic cases were sensitive to allergens from the gut.

(iii) When the evidence of allergy in the cases sensitive to external excitants is analysed

it is found that out of ten of the European cases three were proved to be definitely allergic by a positive dermal test and the fact that they gave a history that the excitant brings on the attack. In seven cases the presence of the allergy was presumed from a history of inheritance, or a positive dermal test or the disease started in childhood. Amongst the Indian cases, allergy was definitely established only in one case out of twelve, in others (who were really bronchial cases) the

organisms isolated from the stools, depending on whether the case was one of amœbic infection, hookworm disease or some post-dysenteric lesion of the gut. The allergic cases when found to be sensitive to an external allergen were advised to avoid the particular excitant and in this group one case was successfully treated by repeated injections of the excitant (this case was sensitive to seed dust and was desensitised by repeated injections of the sterile extract made from the dust). The

TABLE XI

	Total number of cases	Number of cases treated	Relieved	Much improved	Improved	Not improved	Reasons for not treating
Bronchial cases ..	79	49	28 (four relapsed).	12	8	1	1. Cases with open tuberculous lesion and tubercle bacilli in sputum. Referred to elsewhere. 2. Cases did not turn up.
Gram-negative-bacilli cases.	27	21	13 (one relapsed).	3	4	1	Cases did not turn up.
Allergic cases ..	44	28	16 (one relapsed).	1	8	3	1. Allergic cases having no symptoms in the hospital. 2. Cases did not turn up.
TOTAL ..	150	98	57 (six relapsed).	16	20	5	

presence of allergy was presumed from the history of inheritance, a positive dermal test or the early age of onset. This fact further demonstrates the rarity of asthma of allergic origin amongst Indians. In this connection it is interesting to note that Coca, Deibert and Menger (1922) found that the American Indian did not suffer much from these allergic phenomena, asthma and urticaria as compared with the white races. An experimental study of the occurrence of serum disease in twenty-six volunteers, pure-blooded American Indians—indicates that the Indian race was much less susceptible to that condition than the white races.

(20) The results of treatment are given in table XI.

The bronchial cases were treated with a course of autovaccine prepared from the sputum, the Gram-negative-bacilli cases were treated with a vaccine made from that organism. It will be seen that the benefit derived from the vaccine treatment in both the groups is about the same. The allergic cases of gut origin were treated with emetine, carbon tetrachloride or autogenous vaccine prepared from the pathogenic

mixed bronchial and allergic cases were treated with autogenous vaccines made from the sputum as in bronchial cases.

REFERENCE

Coca, A. F., Deibert, O., and Menger, E. F. (1922). *Journ. Immunol.*, Vol. VIII, p. 201.

GRAM-NEGATIVE-BACILLI ISOLATED FROM THE SPUTUM IN CASES OF ASTHMA

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Introduction.—Walker (1919) recovered a Gram-negative-bacillus from the sputum of one out of 74 cases of asthma; the organism resembled the coli type of bacilli in its sugar reactions. Rackemann (1920) investigating the bacteriology of the sputum in 40 cases of asthma isolated a Gram-negative-bacillus in two cases. Rackemann and Graham (1923) in the sputa

from 29 cases of asthma found a Gram-negative-bacillus predominating in one case. Thomas, Famulener and Touart (1924) found a Gram-negative-bacillus in 30 out of 180 cases of asthma. Noranha (1926) reported two cases of asthma successfully treated with a vaccine made from Gram-negative-bacilli isolated from the sputum. Eyre (reported by Knott, 1929) was the first to call special attention to the occurrence of these Gram-negative-bacilli and the fact that by vaccine injection or intracutaneous testing patients could often be shown to be specially sensitive to them. He found that the bacillus grew well at 22°C. and called it the 'asthma bacillus'. Knott, Oriel and Witts (1930) isolated in 48 cases out of 132 sputa examined these Gram-negative-bacilli by Eyre's technique, i.e., incubating the sputum on blood-agar plates at 22°C. Knott and Oriel (1930) considered that these bacilli might be producers of a histamine-like substance which is present in many asthmatic sputa.

SIGNIFICANCE OF THE BACILLUS

(1) *Histamine production*.—Knott, Oriel and Witts (1930) studied 22 strains of these bacilli in detail and found 10 strains to be histamine producers. Knott and Oriel (1930) obtained a histamine-like effect from extracts of various asthmatic sputa. Referring back to the bacteriology of these particular sputa they found that many showed in the bronchial plugs numerous Gram-negative-bacilli. The broth culture extracts of these bacilli gave a histamine-like effect similar to that obtained from the sputum itself. They think that the histamine-like substance demonstrable in the plugs may have arisen as a result of the growth of these bacilli within the small bronchial tubes. In this connection it is interesting to note that Harkavy (1930) had already shown the presence of a spasm-producing substance in asthmatic sputa. Oriel (1932) considers that the local production of histamine in the bronchi in addition to causing contraction of the plain muscle surrounding the bronchi would also tend to increase the permeability of the epithelium lining the bronchioles, and facilitate the entrance of foreign proteins and possibly bacteria. Professor McDowall (1932) speaking at the first International Congress on Asthma drew attention to this local production of bronchospasm through the liberation of histamine in the bronchi by these bacilli.

(2) *Cutaneous sensitivity to emulsion of the organism*.—Knott, Oriel and Witts (1930) found that skin tests made with emulsion of these organisms gave positive results in 74 per cent. of patients from whom they were isolated and in only 11 per cent. of patients in whom they were absent. In cases tested for cutaneous sensitivity to emulsions of cocci obtained from their asthmatic plugs no positive reactions were obtained.

(3) We have shown that in asthmatic cases with Gram-negative-bacilli infection there is usually a very high blood eosinophilia and that they form a separate clinical group.

(4) Knott, Oriel and Witts (1930) found eosinophiles in the sputum in seven-eighths of his cases with Gram-negative-bacillus infection while only one half of other cases showed eosinophiles in the sputum, i.e., out of 48 cases with Gram-negative-bacillus 42 showed eosinophiles in the sputum and 6 did not; of the remaining 84 cases only 43 showed eosinophilia in the sputum and 41 did not.

We do not find any correlation between Gram-negative-bacillus infection and sputum eosinophilia; to this point we shall refer later.

In a series of 150 cases we obtained Gram-negative bacilli in 27 cases, i.e., 18 per cent. of our cases.

DESCRIPTION OF THE BACILLUS

Morphology.—Non-sporing, short thick rods, straight or slightly curved, occurring singly, in pairs or in small chains. Very pleomorphic in cultures, when diplococcal or very long filamentous forms are seen.

Motility.—Non-motile.

Staining reactions.—Gram-negative, non-acid-fast, capsule not seen.

Cultural characters.—Grows well on ordinary media at our room temperature (27° to 32°C.) and at 37°C. Cultures kept in the cold-room (21° to 23°C.) did not grow.

Gelatin stab (with 1 per cent. agar):—No surface growth. Growth along stab. No liquefaction.

Agar slant:—Fine opaque colonies with transmitted light, which coalesce together to make a streak. Growth moderately profuse.

Blood-agar slant:—No hæmolysis, fine transparent growth.

Serum:—No visible growth. Smear shows scanty growth.

Nutrient broth:—Slight turbidity with a watered-silk appearance, deposit at the bottom.

Potato:—No visible growth, on staining short diplococcal and bacillary forms are seen.

Sugars:—No gas is formed in any of the sugars tested, acid is usually formed in glucose, levulose, galactose, maltose, saccharose and dextrin. Usually no acid is formed in lactose, dulcitol, salicin and inulin. Mannite is usually fermented with the production of acid, but when the strain is kept for some time the subcultures do not attack mannite. Sugar reactions for the 15 strains studied are given in table I.

Litmus milk:—Usually unchanged. Slight acidity in one case and acid and coagulation in another—in this case lactose was also fermented with production of acid.

Pathogenicity.—Non-pathogenic to mice, rats and rabbits by intraperitoneal and intravenous injections.

Heat.—Heating at 50°C. for 15 minutes kills the organisms.

Histamine production.—This was studied in 8 strains with negative results. As we obtained negative results with cultures in ordinary broth,

fermentation, and is allied to the coli type of bacilli. No gas is produced in any sugar by any of the strains studied by us.

TABLE I.

A statement showing the sugar reactions and motility of 15 strains of Gram-negative-bacilli (reactions in laevulose, galactose, arabinose, inulin and dextrin were studied in only 5 strains).

No.	Motility	Lactose	Glucose	Maltose	Saccharose	Mannite	Dulcite	Salicin	Litmus milk	Lævulose	Galactose	Arabinose	Inulin	Dextrin
1	—	O	A	A	A	A	O	O	As	A	A	A	O	A
2	—	O	A	A	A	A	O	O	O
3	—	O	A	O	A	A	O	A	O
4	—	O	A	O	A	A	O	A	O
5	—	O	A	A	A	A	O	O	O
6	—	O	A	A	A	A	O	O	O
7	—	O	A	A	A	A	O	O	O
8	—	O	O	As	As	As	O	O	O	O	A	O	O	A
9	—	O	A	A	A	A	O	O	O	A
10	—	O	A	A	A	A	O	O	O	A
11	—	O	A	A	A	O	O	O	O	A	A	A	O	A
12	—	O	A	A	A	O	A	O	O	A	O	O	O	A
13	—	O	A	A	A	O	O	O	O
14	—	O	A	A	A	O	O	O	O
15	—	A	A	A	A	A	A	O	Ac

A = acid in sugar media.
Ac = acid and coagulation.

As = slight acid.
— = non-motile.

O = no acid or gas in sugar media.

cultures made in serum broth and Martin's broth were also tested with negative results.

When we come to compare the Gram-negative-bacilli isolated in our study to those isolated by others we note that:—

1. No description is given of the organisms except by Walker and Knott.

3. The 22 strains studied by Knott showed a great variation as regards the sugar reactions, which are shown in a compressed form in table II.

His 22 strains can be divided into two groups—non-lactose fermenters and lactose fermenters. Non-lactose fermenters can be further divided

TABLE II.

		Lactose	Glucose	Saccharose	Maltose	Mannite	Dulcite	Litmus milk	
6	4 strains .. 1 strain .. 1 strain ..	— — —	A A A	— — —	— — A	— — —	— — —	Alk. A A	11
5	2 strains .. 1 strain .. 2 strains ..	— — —	AG AG AG	— — —	A AG AG	— — AG	— — —	A A A	11
3	1 strain .. 1 strain .. 1 strain ..	A A A	A AG AG	— — AG	A AG AG	— AG AG	— — —	A A A	11
8	7 strains .. 1 strain ..	AG AG	AG AG	— AG	AG AG	AG AG	— —	A A	11

A = acid.

AG = acid and gas.

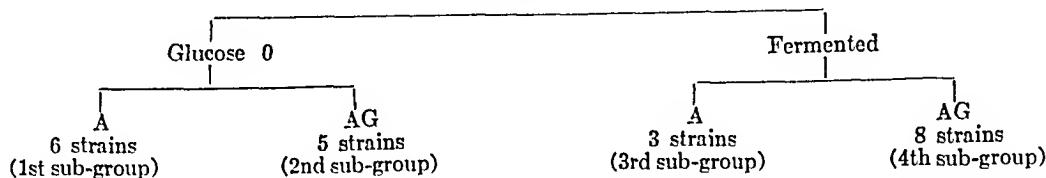
Alk. = alkaline.

2. The one strain isolated by Walker produced acid and gas in the sugars undergoing fermentation, and is allied to the coli type of bacilli. No gas is produced in any sugar by any of the strains studied by us.

glucose. Lactose fermenters can similarly be divided according to whether they produce (A) or (A & G) in lactose.

It will be seen while our strains differ widely from Knott's, all of our strains resemble each other rather closely, thus leaving out the lactose-

LACTOSE



For comparison we give the sugar reactions in a compressed table for the 15 strains studied by us (table III).

We see that :—

(1) Fourteen strains out of the 15 are non-lactose fermenters.

(2) The one lactose fermenter produces only acid in lactose and other sugars, amongst Knott's strains there is one strain that is similar to this but differing in not fermenting saccharose and mannite and in producing only acid in milk while our strain produces acid and coagulation.

fermenting strain and the one non-lactose-fermenting strain not fermenting glucose we find that :—

(a) All the 13 strains ferment glucose and saccharose, and none of them has any action on milk.

(b) All but 2 ferment maltose and all but 5 ferment mannite.

(c) Dulcitate and salicin are not as a rule attacked; only one strain ferments dulcitate and the two strains that do not ferment maltose ferment salicin.

TABLE III.

		Lactose	Glucose	Maltose	Saccharose	Mannite	Dulcitate	Salicin	Litmus milk
	1 strain ..	—	—	As	As	As	—	—	As
13	2 strains ..	—	A	—	A	A	—	A	—
	1 strain ..	—	A	A	A	A	A	—	—
	6 strains ..	—	A	A	A	A	—	—	—
	4 strains ..	—	A	A	A	—	—	—	—
	1 strain ..	A	A	A	A	A	—	A	Ac

A = acid.

As = slight acid.

Ac = acid and coagulation.

— = no reaction.

(3) Amongst the 14 non-lactose fermenters there is one strain which does not attack glucose and produces very slight acid in other sugars.

(4) The remaining 13 non-lactose fermenters produce acid in glucose and belong to the first sub-group in Knott's strains. However, they differ from his 6 strains in this sub-group as under :—

(a) None of our strains produce any change in litmus milk; 4 of his strains make it alkaline and two acid.

(b) All of our strains ferment saccharose; none of his 6 strains attack this sugar.

(c) Eight of our strains ferment mannite; none of his six strains attack this sugar.

(d) Eleven of our strains ferment maltose; only one of his strain ferments this sugar.

(e) We have not been able to demonstrate a capsule in any of our strains; Knott finds a capsule in 2 out of 6 strains.

(f) All his strains grow well at 22°C.; we did not get any growth at 22° to 23°C.

Classification of the bacillus.—So that these 13 strains can be put together in the genus *Eberthella* under the tribe *Bacteriæ* in the family *Bacteriaceæ*. In its specific characters the organism is nearest to *Eberthella phaffi*, the causative organism of fowl typhoid, being non-motile, a non-lactose and non-dulcitate fermenter, forming acid in glucose, in saccharose and usually in mannite, and producing no change in litmus milk.

Its pleomorphic character makes it resemble superficially *Klebsiella pneumoniae* Friedländer from which it differs in the following details :

(1) No capsule is seen.

(2) Growth not so abundant as in case of *Klebsiella pneumoniae*.

(3) No gas is produced in any of the sugars fermented.

(4) Non-pathogenic to mice, rats and rabbits. *Klebsiella pneumoniae* is highly pathogenic to mice; rabbits are less susceptible.

TABLE IV.
Details of cases having *Gram-negative-bacilli in sputum.*

Serial number	Case number	Age and sex	Duration of illness	Age at onset	Effect of season or weather	Pre-asthmatic state	Blood count		Sputum eosinophiles	Treatment	Result
							Total leucocytes	Total eosinophiles			
1	17	34 F.	19 years	15	Worse in summer	..	12,000	960	No.	Auto-vaccine sputum.	Relieved.
2	26	55 M.	9 "	45	..	Occasional colds	7,000	420	No.	Do.	Much improved.
3	29	38 M.	10 "	28	Worse in winter and rains.	..	13,400	6,618	No.	Not treated	..
4	30	21 M.	3 months	21	..	Severe bronchitis for 1 year preceding.	16,000	9,600	..	Auto-vaccine sputum.	Relieved.
5	31	18 F.	3 years	15	..	Bronchitis 1 year	25,400	5,350	A few eosinophiles.	Do.	Do.
6	36	33 M.	14 "	19	Worse in winter	..	16,000	5,760	Some eosinophiles	Do.	No improvement (old tuberculous lesion, right apex).
7	38	38 M.	4 "	34	..	Running of nose for some time.	8,000	1,360	No.	..	Not treated.
8	40	25 M.	1 year	24	..	Irritation of nose with occasional bleeding. Pneumonia 2 years before. Bronchitis after pneumonia.	25,000	13,500	Eosinophiles make up 50 per cent. of cellular exudate.	Auto-vaccine sputum.	Much improved.
9	52	32 M.	1½ years	30½	..	Pneumonia started just after pneumonia.	16,000	9,400	Do.	Do.	Improved.
10	57	30 M.	1½ "	28½	..	Pneumonia 1 year before asthma.	16,000	6,720	No.	..	Relieved. Had a relapse 10 months later.
11	58	45 M.	9 "	36	..	Pneumonia, pleurisy.	16,000	3,000	Several eosinophiles.	..	Not treated.
12	65	30 F.	10 "	20	Worse during the rains.	Pneumonia. Asthma started just after pneumonia.	10,000	800	No.	..	Do.

13	68	27 M.	1 year	26	..	Bronchitis 1 year before starting asthma.	9,000	6,000	..	Auto-vaccine sputum.	Improved.
14	77	42 M.	6 years	36	..	Pneumonia 1 year before starting asthma.	17,000	5,000	Most of the cells were eosinophiles.	Do.	Much improved.
15	79	36 M.	20 "	16	Worse in winter	..	8,000	800	Do.	3 doses auto-vaccine.	Improved.
16	84	28 M.	5 "	23	Worse in winter	..	16,000	10,240	No.	..	Not treated.
17	91	30 M.	10 "	20	During rains only	Bronchitis for 5 years.	10,000	1,000	No.	Auto-vaccine sputum.	Relieved.
18	93	20 M.	2 "	18	During rains only	Tonsils removed at age of 5 and again at 20. Adenoids removed at age of 12.	9,000	4,000	No.	Do.	Improved.
19	100	30 M.	12 "	18	8,000	2,000	..	Do.	Relieved.
20	110	35 M.	6 months	34½	..	Chronic colds and sore throat.	7,000	700	Eosinophiles make up more than 50 per cent.	Auto-vaccine sputum. Nose attended to.	Do.
21	120	32 M.	10 years	22	Worse in winter	Chronic bronchitis.	6,000	1,440	No.	Auto-vaccine sputum. Hook-worm infection treated.	Do.
22	125	21 M.	8 "	13	In winter only	..	15,000	6,000	No.	Auto-vaccine sputum.	Do.
23	127	42 M.	7 "	35	In extremes of temperature.	Bronchitis for 3 years.	11,000	1,000	No.	Auto-vaccine supplied.	..
24	138	24 M.	1 month	24	7,000	700	No.	Auto-vaccine sputum.	Relieved.
25	139	36 M.	6 years	30	..	Pneumonia. Asthma started just after pneumonia.	25,000	16,000	No.	Do.	Do.
26	140	30 M.	5 "	25	15,000	7,000	No.	Do.	Do.
27	142	52 M.	37 "	15	..	Bronchitis	7,000	770	No.	Do.	Do.

Relieved

= Completely relieved of symptoms.

Much improved

= Intervals between attacks considerably increased, and the duration and acuteness of attacks lessened.

Improved

= Definite improvement but not very marked.

Not improved

= No improvement at all.

Before completing the description of the bacillus it may be worth while to refer to the few experiments carried out with a view to observing if the injection of the organism has any effect on the blood or tissue eosinophilia.

1. Broth culture of the organism injected subcutaneously in mice. Result—no local eosinophilia.

2. Broth culture of the organism injected into the pleural cavity of mice. Result—no local eosinophilia.

3. Filtrate from the broth culture injected intradermally in one patient (repeated injections). Result—doubtful increase in the blood eosinophilia, i.e., variations from none to 280 per c.mm.

A table detailing of the cases with the Gram-negative-bacilli in the sputum is given.

POINTS FROM THE TABLE.

(1) Sputum eosinophilia. Out of 27 only 8 show eosinophiles in the sputum (out of the series of 150 cases 36 show eosinophilia of the sputum, and of the 79 cases of bronchial asthma not associated with Gram-negative-bacillus infection only 16 show eosinophiles in the sputum), so that cases with Gram-negative-bacillus infection have a higher incidence of sputum eosinophilia than other cases, but we have not found the incidence as high as in Knott's cases; he finds seven-eighths of his cases showing sputum eosinophilia.

(2) High blood eosinophilia. This is not referred to by Knott, but in a personal communication he says 'all the patients infected with bacillary strains have shown eosinophilia (blood and sputum) or other manifestations of allergy'. This high blood eosinophilia has been shown by us to be of diagnostic importance.

(3) Out of 27 cases 13 gave a history of inheritance (in the total series of 150 cases only 40 gave a hereditary history, and out of 79 bronchial cases not due to these Gram-negative-bacilli, only 15 gave a history of inheritance).

(4) Age of onset. In 22 cases the age incidence varies from 11 to 30 years, and in 5 the age of onset was above 30 years and of these 4 started within 36 years; there was only one patient who commenced his asthmatic attack at 45 years. (In 38 of the 79 bronchial cases without infection with the Gram-negative-bacillus the age of onset was above 30.)

(5) Effect of season. Out of 27 only 10 cases gave a history of seasonal variation and of these 7 were worse during the winter and rains or got the attacks only at this season, one was worse in summer, and two worse during extremes of temperature. (Of the 79 bronchial cases not infected with the bacillus 35 shows seasonal variation and, of these 35, 29 were worse during the winter and rains, or got attacks only at those seasons.)

(6) Pre-asthmatic state. Of the 27 cases 18 or two-thirds gave histories of a previous illness,

i.e., 8 pneumonia, 7 chronic bronchitis, 2 nose and throat troubles and 1 dysentery. (Of the 79 bronchial cases without infection with this bacillus 52 gave a history of previous illness, i.e., 16 pneumonia, 30 chronic bronchitis, 4 nose and throat, 1 dysentery and 1 urticaria. Of the 22 gut allergic cases as many as 8 have a history of previous dysentery—the importance of the fact will be discussed in another paper.) A history of a previous pneumonia attack is more common in these cases than in the bronchial cases not infected with these bacilli.

(7) Result of treatment. Of the 27 cases 22 were treated (5 did not come for treatment) and the results of treatment are only available in 21 cases. Of these 21, 13 were completely relieved of their symptoms (there was 1 relapse in these 13), 3 were much improved, the intervals between the attacks having increased and the duration of the attacks lessened, while 4 were only slightly improved and 1 not improved at all. (In bronchial cases without the Gram-negative-bacillus infection, of the 49 cases treated 28 were relieved, 12 much improved, 8 improved, and 1 not improved.)

The following additional points which are not included in the table are worth mentioning.

(1) The co-existence of other allergic manifestations. In our total series of 150 cases of asthma there was only one case suffering from allergic dermatitis, and it was one of these Gram-negative-bacillus cases.

(2) History of previous allergy. Out of this series only 2 gave a history of having suffered from urticaria, and two suffered from sneezing and running of the nose before getting asthma. (In the total series of 150 cases 11 had suffered from urticaria previously.)

(3) Dermal tests were performed with extracts of the different hairs, feathers and foods in general use, when indicated in the history; grass pollens were included. Of the 25 cases tested only 3 gave positive results, one with cattle-hair, one with several foods and one with Timothy-grass pollens and milk. The positive tests did not prove to be of any value from the treatment point of view. (In the 67 bronchial cases without the Gram-negative-bacillus infection in whom dermal tests were done 57 were negative, 3 doubtful and only 7 positive.)

(4) Von Pirquet tests. Of the 16 cases where this test was done only 7 were positive. (In the bronchial cases without this bacillus infection 35 out of 60 were positive.)

(5) Evidences of pulmonary tuberculosis. There were only 3 cases showing any evidence of this disease and all these were old healed lesions detected in the skiagrams. (In the 79 bronchial cases there were 15 tuberculous cases of which one was an early case, 4 with well advanced lesions, and 10 with old healed lesions.)

(6) In none of the 27 cases did a change of place or food have any effect on the attacks.

Discussion.—Relation of the bacillus to asthma.

As already mentioned Oriel (1932) considers that the local production of histamine in the bronchi in addition to causing a contraction of the plain muscle surrounding the bronchi would also tend to increase the permeability of the epithelium lining the bronchioles and facilitate the entrance of foreign proteins and possibly bacteria.

Knott in a personal communication says that he thinks that the weight of evidence is that the organisms cannot themselves provoke an attack of asthma in a perfectly normal person, but only in those whose bronchioles are already irritable and on the verge of contraction; in allergies these infections are therefore particularly potent in precipitating clinical attacks or maintaining chronic asthma.

Our cases do not fall under the allergic group as is evident from the results of dermal tests and from the absence of any other associated allergy or history of previous allergy. We have not succeeded in demonstrating any histamine-like effect in cultures of the organisms isolated by us. The only thing we can say at present is that in our study of 150 cases of asthma we have come across 27 cases which constitute a clinical group amongst the bronchial cases characterised by high blood eosinophilia and presence of pleomorphic Gram-negative-bacilli in smears and cultures of sputum.

SUMMARY.

1. Morphological and cultural characters of the Gram-negative-bacilli isolated from the sputa of asthmatics are described. The classification and significance of these bacilli are discussed.

2. A table of the cases showing the Gram-negative-bacillus in their sputa is given and the following conclusions made.

(a) All the cases show a high blood eosinophilia and less than one-third show a sputum eosinophilia.

(b) About half the cases gave a history of heredity.

(c) Age of onset in more than three-quarters of the cases varies from 11 to 30 years.

(d) The response to treatment by vaccine made from these organisms is the same as in bronchial cases due to other bacteria.

(e) In only one case was there any other co-existing allergic manifestation, but two gave a history of having suffered from urticaria and another two patients suffered from sneezing and running from the nose before getting the asthma.

(f) The dermal tests are of no value in the diagnosis of these cases.

(Continued at foot of next column)

BRIEF NOTE ON THE RESULTS OBTAINED WITH ANTI-GAMETOCYTE TREATMENT ONLY, WITHOUT ANTI-LARVAL MEASURES

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THE work of Barber, Komp, and Newman (1929) showed that very small doses of plasmoquine (0.01 gramme twice a week) were sufficient to prevent gametocytes infecting anophelids. The writer of this note has made a large number of practical trials of this method on estates, endeavouring to keep the coolie population free from malaria by the use of the anti-gametocyte action of plasmoquine *only*. For a variety of reasons, which need not be described here, many of the early experiments failed to produce conclusive results. This year, however, three very carefully controlled experiments were carried out during the malaria season, the results of which it is desired to describe briefly. Before doing this, it should be stated that the application of the prophylactic dosing *only* to estates can be carried out in two separate ways, (1) dosing two or three times a week of all members of the community for a period of 8 to 12 weeks during the period of active spread of malaria, and (2) in excessively bad areas where anti-larval measures happen to be impossible, dosing the whole community with quino-plasmoquine, two doses a week, year in and year out. It is intended in this brief note to give some results of both kinds of work.

As regards the first class, the following estates were treated to two (in a few cases three) doses a week of quino-plasmoquine for a period of about ten weeks:—Delwita, Daisy Valley and the lower divisions of Pitakande.

(Continued from previous column)

REFERENCES

- Harkavy, J. (1930). *Arch. Intern. Med.*, Vol. XLV, p. 641.
 Knott, F. A. (1929). *Guy's Hosp. Rep.*, Vol. LXXIX, p. 491.
 Knott, F. A., and Oriel, G. H. (1930). *Journ. Physiol.*, Vol. LXX, p. xxi.
 Knott, F. A., Oriel, G. H., and Witts, L. J. (1930). *Guy's Hosp. Rep.*, Vol. LXXX, p. 421.
 McDowall, R. J. (1932). *Lancet*, Vol. I, p. 1343.
 Noronha, A. J. (1926). *Indian Med. Gaz.*, Vol. LXI, p. 75.
 Oriel, G. H. (1932). *Allergy*. London: John Bale Sons & Danielsson, Ltd.
 Rackemann, F. M. (1920). *Journ. Immunol.*, Vol. V, p. 373.
 Rackemann, F. M., and Graham, L. B. (1923). *Journ. Immunol.*, Vol. VIII, p. 295.
 Thomas, W. S., Famulener, L. W., and Touart, M. D. (1924). *Arch. Intern. Med.*, Vol. XXXIV, p. 85.
 Walker, C. (1919). *Arch. Intern. Med.*, Vol. XXIII, p. 220.

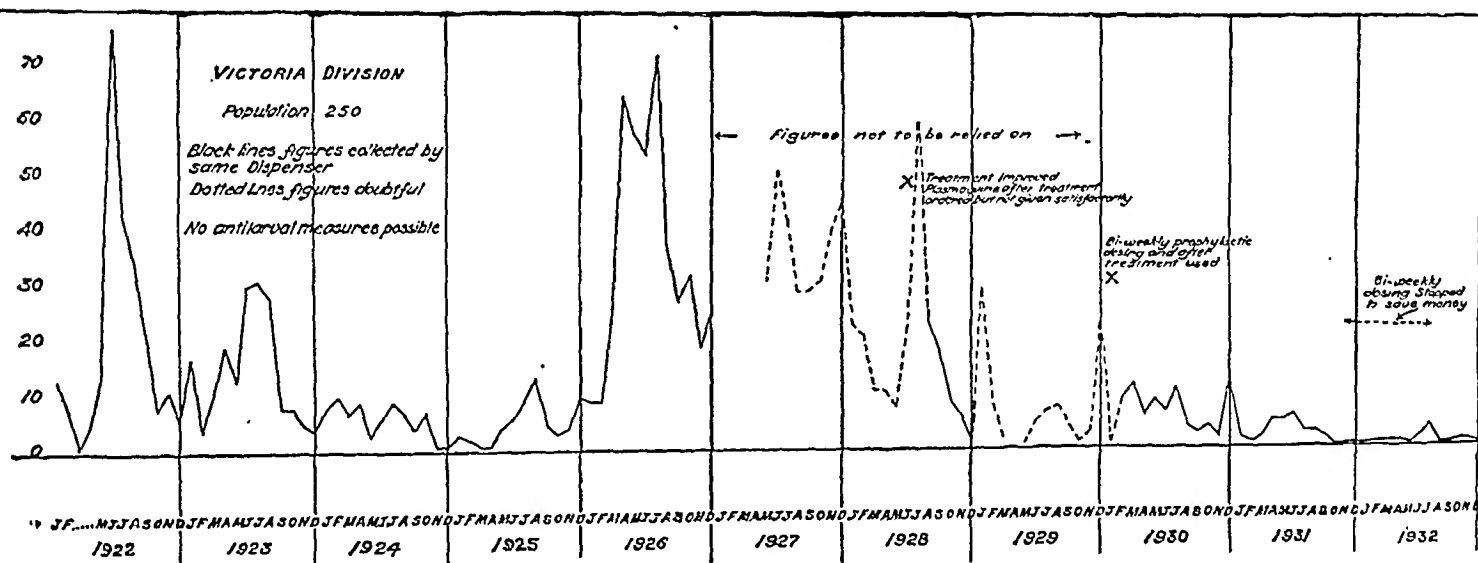
As regards the second class (continuous treatment) these are the two divisions of Mahabirattenne and the Victoria division of Pallakelley.

We will first say something concerning the first group. All of these estates are located in an area of very high endemicity, viz, the Kurunagalla District; the village spleen rate is between 80 per cent. and 90 per cent. at all times of the year; that on estates is considerably lower. The district is situated at the foot of the hills and many streams arising in the hills pass through it; these rivers are the main breeding places of *Anopheles culicifacies*; it is this species which does all the damage.

Delwita.—It is not possible to give in detail the facts regarding the outbreak of malaria on this estate; they can be summarized as follows:—The population of a little under 400 lives in lines on both sides of the Dedru-Oya, which under suitable conditions pours out an enormous number of *Anopheles culicifacies*. This year the conditions were highly favourable for about 8 to 10 weeks during July and

every case that sickened with fever was taken, and a remarkable condition of affairs was discovered, namely, (1) more than half the blood slides showed no parasites at all, although there can be little doubt that the infection was true malaria (anybody who had fever is included in the figures, whether parasites were found or not); (2) two days of 30 grains of quinine cured the patient, in spite of the fact that most of the cases were malignant tertian (*P. falciparum*); there was only one serious case out of the 76, all the others resembling a mild infection of benign tertian, and the number of days absence from work was very small. The outbreak demonstrates a fact which is well known to all malariologists, namely, that when there are a large number of vectors (in this case *Anopheles culicifacies*) extraordinarily few gametocyte carriers are sufficient to cause an outbreak.

Daisy Valley.—The estate of Daisy Valley is situated a few miles away, in the same district. There are rivers on both borders, from which *A. culicifacies* larvæ were obtained in large



August; larvæ were plentiful during this period and were caught regularly by our assistant; malaria itself was very prevalent in the neighbouring villages. The dosing was very carefully done by the dispenser, who is a conscientious and hard-working man; the scattered nature of the lines rendered the work of dosing the labour force rather difficult; a few babies in arms were omitted, the parents keeping the children hidden away. The results of the campaign were in a measure satisfactory, but were only partially successful; 20 per cent. of the total labour force sickened with malaria. Half way through the epidemic, we discovered two or three babies under 18 months of age had not received their regular dose, and it is highly probable that the local *anopheles* obtained their malarial parasites from these. A blood slide of

numbers. The population on the estate is 105 souls. Two doses a week were administered by the superintendent himself, because the estate being small no separate dispenser is kept. There was not a single case of malaria during the whole period, and practically no sickness of any kind whatever. The neighbouring villages suffered severely. Half way through the dangerous time, the blood of 34 children was examined. They were free from parasites, with the exception of five; there were only two dangerous individuals, both showed quartan gametocytes, amongst this group. The measures were a success and kept the labour force entirely free from malaria during a moderately severe outbreak among the civil population.

Pitakande.—The estate of Pitakande is in the same district and only a few miles away,

but the results obtained on this estate are nothing like as convincing as on the previous two, for two reasons, namely, (1) several years ago, at my recommendation, all the lines near the river were pulled down and rebuilt on a better situation, and (2) most of the lines are on high ground at the foot of the hills, not on the plains themselves. Prophylactic dosing was given during the bad period of October and November to all, except the top division. No cases of malaria resulted, but many estates and villages in the neighbourhood suffered severely.

Dealing now with the second class of work, it is necessary to say that the two divisions of Mahabiratenne and Victoria division are situated on the angle between the two large rivers, the Hulu Ganga and Mahaweli Ganga. The distances of the three divisions from the river are as follows :—

The central division of Mahabiratenne is about two and a half miles from the river, spleen rate in 1927 (before measures were adopted) 12 per cent. The Henegahawela division of Mahabiratenne is about three-quarters of a mile distant, spleen rate in 1927, 25 per cent. Victoria division is three to four hundred yards distant, spleen rate in 1927, 100 per cent.

There are practically no minor breeding places on the three divisions. All small streams and puddles dry up within ten days of the cessation of the rains. It is quite impossible to do anything in the shape of anti-larval measures to the Hulu Ganga and Mahaweli Ganga, consequently, the only measure which will give the slightest hope of success is continual dosing. Regular dosing, twice a week, year in and year out, was carried on on the two divisions of Mahabiratenne from June of 1930, and on the Victoria division from January of 1931. The results since then are given as follows :—

	Popula- tion	TOTAL CASES FOR THE YEAR		
		1930	1931 *	1932 *
Central division, Mahabiratenne.	325	66	20	5
Henegahawela division of Mahabiratenne.	300	62	24	6
Victoria division of Pallakelley.	250	80	29	10

* Blood films taken in all cases.

During the years 1930 and 1931 there have been two violent epidemics in the civil population; there was very little ill-health in 1932. The labour in Mahabiratenne and Victoria entirely escaped these outbreaks, as the figures above and the chart show.

In a brief statement like this, it is impossible to convey any idea of the change that has taken place within three years. The children are now

fat and healthy and practically free from parasites; the out-turn to work amongst the adults now is well over 95 per cent., and the saving to the company is very great. In 1928, conditions were lamentable.

During the spring of 1932 our investigations showed that *Anopheles culicifacies* was decidedly rare, so that from December 1931 to July 1932, no prophylactic dosing was considered necessary. This course was adopted largely in the interest of economy, as the companies owning the estates were very anxious to save every penny on account of the condition of the market. No ill-results whatever have occurred from this cessation of the dosing up to date, but it must be stated that 1932 was a healthy year in this district; the malaria figures in the civil population were low.

The examination of the blood of the children on Victoria has shown that, since the use of plasmoquine, the only parasite that survives is 'quartan'. At the last blood slide examination, November 1932, 10 per cent. of the children had quartan parasites in their blood; Atcbrin is being tried to remove these.

Conclusions

In spite of the somewhat small number of these trials, the results show that it is possible to control entirely the spread of malaria by careful anti-gametocyte work. This appears to be quite easy in cases in which the prophylactic doses are given over long periods, as a regular procedure. When given over a short period of great danger, they are equally successful, provided certain conditions are rigidly adhered to.

2. If a high degree of success is wished for, a thorough comb-out of gametocyte carriers in the labour force must be undertaken. This usually means examining the blood of all children and adults in bad health, babies in arms to receive particular attention, because of the likelihood of these missing the bi-weekly dose.

3. The search for and cure of gametocyte carriers should always be undertaken at least a month ahead of the onset of the dangerous period.

4. In a community receiving two doses of quino-plasmoquine a week, those who sicken with fever show extraordinarily few malaria parasites (trophozoites or schizonts) in the peripheral circulation. Malignant tertian and benign tertian gametocytes will never be found if the dose is taken regularly. Quartan parasites and gametocytes are much more frequently met with and are much less acted on by the plasmoquine, than the other two.

5. Two doses of quino-plasmoquine a week, causes the attack, even of malignant tertian, to be mild in character. The duration of the fever is usually two to four days, instead of eight to twelve days, and profound disturbance in health is only observed in very susceptible newcomers to the district.

6. The only objection to the regular treatment of a whole labour force is the trouble and expense involved. The cost for a whole year is much less than that occasioned by a severe outbreak of malaria.

The writer apologises for the paucity of the evidence brought forward in support of the above statements. Careful graphs are kept in the office of the Malaria Control Scheme, going back for a large number of years. They show the sickness rate in the civil population as obtained from the local hospitals, side by side with that of our estates. They are of very great interest and importance, but they are too large for suitable reproduction in a medical journal. If any of the readers are interested in a more detailed account of these occurrences, the writer is in a position to send them a copy of the records in our office, which gives all the evidence, and contains copies of the graphs. Any who would care to have these, will be supplied if application is made to Lieut.-Col. W. W. Clemesha, I.M.S. (retd.), Malaria Control Scheme, 'Daytona', Kandy (Ceylon).

REFERENCE

Barber, M. A., Komp, W. H. W., and Newman, B. M. (1929). *Pub. Health Reports*, Vol. XLIV, Part I, p. 1409.

CERTAIN INJURIES OF THE WRIST THAT ARE FREQUENTLY OVERLOOKED

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SOME of the injuries of the wrist and foot which appear trivial often pass undiagnosed. These injuries are as common in the civilian as in soldier, but the civilian, thinking the lesion to be of very minor nature, hardly ever consults the doctor. Even when he does so, the average general practitioner, not having the benefit of *x-ray* at his disposal, is liable to miss the exact pathological lesion. Whereas every case of injury in the army, however trivial it may be, is seen by a medical officer who has an *x-ray* apparatus at his disposal to confirm his diagnosis. The following injuries are discussed in this paper, some of these are common, others rare.

I. Sprain of the carpal scaphoid and semilunar.

II. Fracture of the carpal scaphoid.

III. Fracture of semilunar.

Of these, fracture of the scaphoid is very common and has been described in detail. Only a passing mention has been made of the others. Dislocation of the semilunar has not been included, as the condition is more or less evident on clinical examination.

Before describing the injuries of the scaphoid and semilunar, let us very briefly recapitulate the anatomy and physiology of these two

bones. The scaphoid is most liable to be injured on account of its shape and position. Its shape is like that of a rod the shaft of which is first curved vertically (body) and then its lower end bent perpendicularly (apophysis). Consequently there are two curves, one vertical to fit on to the head of the os magnum and the other antero-posterior formed by the junction of the apophysis and body.

The semilunar is crescentic in shape. The anterior ligament or ligamentum arcuatum is the only strong ligamentous attachment of this bone. Its concave surface fits badly with the head of the os magnum and the beaks, anterior and posterior, are not long enough, hence the bone is easily displaced.

The bones of the carpus are very badly nourished, and the vessels are supported in the ligaments. So when the latter are ruptured, there is always trouble with the nutrition of the bone.

Radiography.—Two plates must always be taken for a correct diagnosis. One antero-posterior and another lateral. For the first the posterior surface of the forearm is placed against the plate and the rays are directed to the centre of the radio-carpal space. For the second, which is more difficult to take, the radius is placed against the plate with the hand in the same plane as the forearm. This can be done by turning the arm and making the patient bend the body, i.e., the arm being in a position slightly higher than the body. In the profile skiagram the scaphoid looks like a bean. The outline of the semilunar is well marked in the lateral picture and its characteristic form is evident.

I. SPRAIN OF THE SCAPHO-LUNARY JOINT

Destot (1925) classified sprains of this joint into five clinical varieties.

1. Mild and simple; in this only clinical symptoms are present.

2. A more serious type associated with subluxation of the semilunar.

3. Where the subluxation has reduced itself, but the ligaments are torn and small fragments of the bone may later form osteophytes.

4. Old sprains with osseous degeneration.

5. Spring wrist or recurrent subluxation of the scaphoid and semilunar.

In this article only the recent injuries are discussed, so we shall confine ourselves to the first and second types.

Clinical features.—The injury is usually caused by falling on the hyper-extended hand. There is pain and swelling in the anatomical snuff-box. Ecchymosis may be present in the thenar eminence. There is no swelling at the back of the hand and crepitus is absent. The most tender point is just below the styloid process of the radius and the whole of the internal part of the wrist is free. Pain is experienced if the space between the scaphoid and semilunar is pressed between the fingers. If pressure is applied between the scaphoid and trapezium

while the thumb is being moved, acute pain will be felt. The height of the wrist is decreased only in persistent dislocation of the semilunar. Passive movements are invariably limited, particularly bending the hand to the radial side. In subluxation, supination and pronation are also limited.

Radiography.—In the antero-posterior skiagram the scaphoid appears globular and shortened. Its upper extremity overhangs the dorsal surface of the os magnum and throws a marked shadow on the head of the latter. The space between the scaphoid and semilunar is either increased or diminished and the scaphoid appears continuous with the semilunar on which it lies. The side view is more important. The semilunar and scaphoid do not make a continuous carpal condyle which appears bigeminate as the curves of the two bones do not fit into each other. In order to make the lesion apparent a schematic radiogram is given instead of a true x-ray photograph.

Active and passive movements are started after a week.

II. FRACTURE OF SCAPHOID.

Frequency.—It is a fairly common injury. Patterson Brown (1928) reported that 46 cases were treated in the Edinburgh Royal Infirmary in the course of two years. Ross and Wibert, quoted by Destot, state that it represents 9 per cent of all fractures. I saw six cases last year and seven in the last eight months of this year. Forty-three cases of fracture have been treated in the Kohat Military Hospital in the last eight months including seven fractures of scaphoid; in other words it formed about 16 per cent of all fractures treated in the hospital. For this purpose statistics of big civil hospitals do not show the true frequency of the injury, because they deal more with cases of major fractures, and patients with minor injuries seldom report there. Quite a lot depends, of

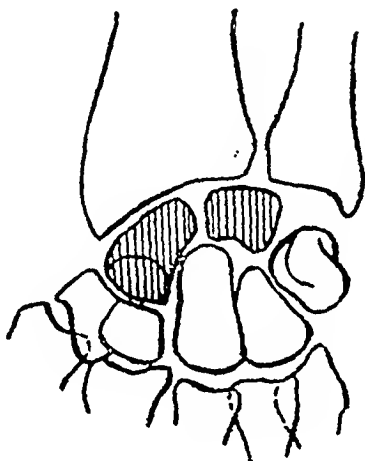


Fig. 1.

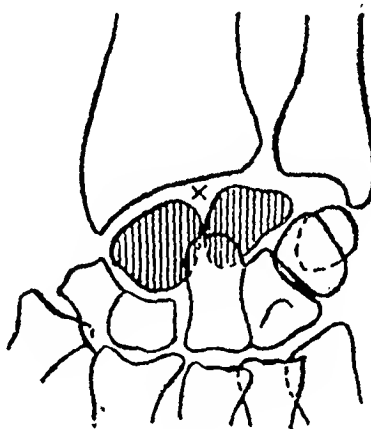


Fig. 2.

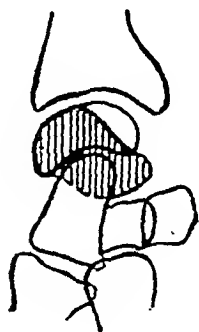


Fig. 3.

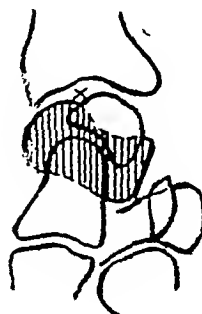


Fig. 4.

The displacement is indicated by the x.

The upper pictures are antero-posterior and lower lateral views.

Figs. 1 and 3 are normal and Figs. 2 and 4 with subluxated semilunar.

Treatment.—The wrist should be immobilised in a small cardboard splint, leaving the fingers free, for one week. The hand is kept slightly inclined to the ulnar side. To reduce subluxation the bone is pressed between the thumb and fingers and the hand is simultaneously extended.

course, on the number of cases that can be x-rayed. The point I want to stress is that it is a very common injury and should always be looked for, because with early diagnosis and treatment complete cure can be assured in 90 per cent, whereas some functional impairment

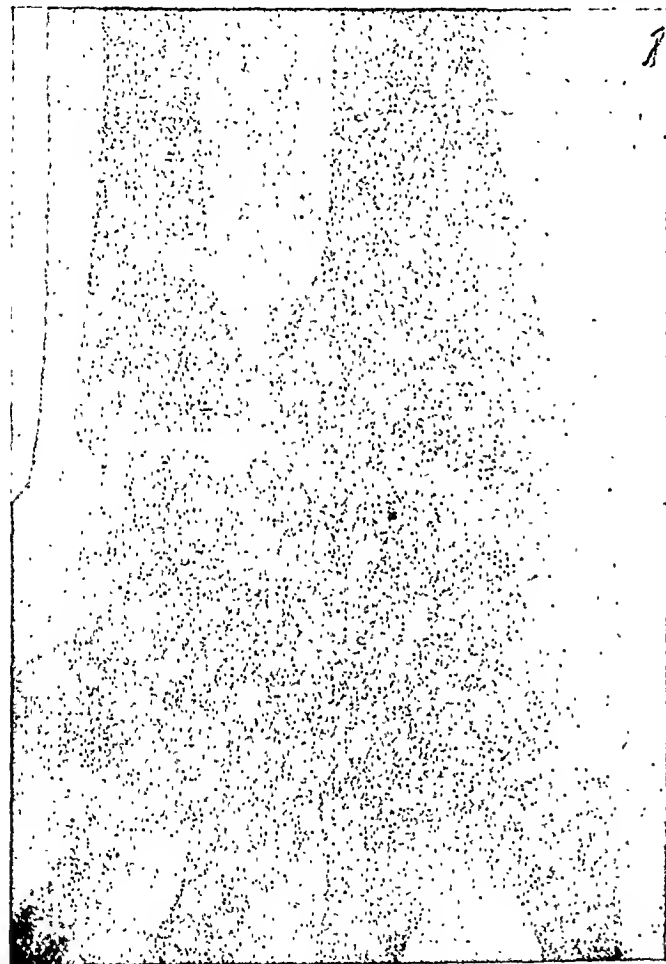
(disability varying from 10 per cent to 40 per cent) is the rule in late cases.

Mechanism of fracture.—The fracture is produced by falls on the hyper-extended hand. In falls of this nature the most direct line of transmission of the body weight is through the scaphoid. It has already been pointed out that this bone has two bent axes and therefore is very liable to break. After impaction it undergoes a bell-like movement (Destot), which brings the upper extremity of the bone posteriorly. At this moment one of the following injuries is liable to occur, according to the exact way in which the body weight is resisted.

trapezium and trapezoid. The force crushes the scaphoid along its long axis producing a transverse impacted fracture of the bone across its middle.

4. If the hand is violently adducted, the external lateral ligament may be torn off the tuberosity of the scaphoid.

Symptoms and diagnosis.—Very few special symptoms are produced by the fracture, and therefore it is so liable to be overlooked. Swelling, pain and tenderness in the anatomical snuff-box are the main symptoms. These are also present in sprains of the wrist joint and fracture of the styloid process of the radius. It should be remembered that fracture of the scaphoid is commoner than sprain of the wrist joint (apart from the sprains of the tendons about the joint). Crepitus can very seldom be elicited. Symptoms of compression of nerve



Skiagram 1.—Incomplete fracture of scaphoid without any displacement.



Skiagram 2.—Complete fracture without any displacement

1. If the limb is not quite perpendicular to the ground (the scaphoid is firmly fixed into the glenoid cavity of radius) the body weight is transmitted through the radius, which is at a mechanical disadvantage and it breaks.

2. If the hand is inclined on the radial side, the scaphoid lies between the radius and os magnum. In this position the head of the os magnum is driven like a wedge into the concavity of the scaphoid and the latter will break across its middle.

3. If the hand is inclined to the ulnar side, the scaphoid comes further out of the wrist joint and lies with the long axis almost vertical between the styloid process of the radius,

trunks or vessels may be produced by the displaced fragment, but this is very rare.

'Tapping pain'.—It was described by Murphy. The hand is held in radial flexion with the fingers flexed. The distal ends of the metacarpal bones are gently struck with a percussion hammer. On striking the third metacarpal, the os magnum is driven against the scaphoid and in case of a fracture even a slight tap causes pain.

Tapping pain in fracture of the scaphoid is most marked when the hand is in radial deviation. In fracture of the semilunar it is most marked when the hand is in ulnar

deviation. No pain is produced in dislocation of the semilunar.

Prognosis.—It is the universal experience that the end results of fracture of the scaphoid which has been overlooked, tend to be a good deal worse than those which are recognised and treated immediately. Prognosis for recent cases is good.

According to Bankert (1932) the treatment advocated by Bohler appears to have improved the end results even in late cases to a great extent.

Treatment.—To reduce the displacement, the hand is flexed and deviated to the ulnar side, pressure is applied at the same time in the anatomical snuff-box, and the broken pieces are

impaired, it was the usual custom to excise the fractured fragments. But recently Bohler has demonstrated that if these cases are kept immobilised in dorsiflexion in a plaster splint for *four to six months*, bony union will occur not only in recent cases but even in late cases. The splint is applied on the dorsal aspect of the hand and forearm, extending from the base of the fingers to the elbow joint with the wrist in slight dorsiflexion and ulnar adduction; this treatment should be carried out in all late cases.

If bony union does not take place even after six months the fragments may be excised, but the results are not very satisfactory.

III. FRACTURE OF SEMILUNAR

It is a rare injury, but recent literature shows that it is not so rare as it was formerly believed



Skiagram 3.—Complete fracture with slight displacement of the upper fragment.

moulded on to the head of the os magnum. A plaster splint is applied and the hand is kept in dorsiflexion for two weeks. The splint is then removed and massage and movements are commenced.

Fractures of the tuberosity, being extra-articular, heal readily after immobilisation for two weeks.

Intra-articular transverse fractures do not heal so readily and may produce a certain amount of functional impairment. Owing to this, specially in those cases which are seen late and in which free movements of the wrist are



Skiagram 4.—Complete fracture with appreciable displacement of the upper fragment and subluxation of the semilunar.

to be. Fracture of the semilunar does not produce any pathognomonic clinical sign and therefore it is very difficult to diagnose. Moreover as it is often associated with small intra-articular fracture of the radius, these often pass unnoticed. The only findings on clinical examination are very slight limitation of the movements of the wrist, slight swelling in the anatomical snuff-box, and a little antero-posterior thickening when the bone is palpated between the fingers.

Tapping pain is most marked on tapping the head of the third metacarpal when the hand is in ulnar flexion.

DIFFERENTIATION FROM DISLOCATION OF THE SEMILUNAR

(a) In dislocation there is appreciable thickening of the wrist due to, (i) prominence on the dorsum formed by the head of the os magnum displaced backwards, and (ii) swelling in front beneath the flexor tendons caused by the dislocated semilunar. In fracture there is swelling of the wrist, but not so much thickening.

(b) Shortening of the carpus as evidenced by the position of the head of the third metacarpal. The head is at the same level or proximal to the heads of the second and fourth metacarpals in dislocation. In fracture the head of the third metacarpal is distal to the others as in a normal case.

(c) In dislocation slight palmar flexion is possible, but dorsal flexion is resisted, whereas in fracture slight dorsal flexion is usually permitted.

(d) Dislocation generally produces symptoms due to pressure on the nerves or vessels. This is hardly ever present in fracture.

(e) Tapping pain is absent in dislocation.

(f) X-ray. In a lateral skiagram in dislocation the concavity of the semilunar does not fit like a cup on the head of the os magnum.

Prognosis.—With early diagnosis and treatment, it is good, but Kienböck's disease is liable to supervene later on.

Treatment.—Germans advocate removal of the bone in all cases. French and British surgeons prefer more conservative methods and advise immediate mobilisation massage and movement in addition to alternate hot and cold douches. If in spite of this the patient does not improve, the bone should be removed. This is further recommended on the ground that Kienböck's disease is liable to supervene.

For removal of the bone British surgeons use a dorsal incision, about 2 inches long, over the lower end of radius and the carpus. Destot prefers a horse-shoe-shaped incision over the middle fold of the flexure of the wrist, between the tendons of palmaris longus and palmaris brevis. He thinks that operation by the posterior route is much more difficult and mutilating. The operation is much easier with a tourniquet round the arm.

REFERENCES

- Bankert (1932). *Manipulative Surgery*, p. 114.
Brown, K. P. (1928). *Brit. Med. Journ.*, Vol. I, p. 591.
Destot, E. (1925). *Injuries of the Wrist*, p. 57.

HYDATID DISEASE IN SOUTH INDIA

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Few cases of hydatid disease have been reported in India. The general impression is that the disease is rare. It is only occasionally that cases appear in the hospitals in large towns, and even these very often are not clearly brought out in hospital reports. The provincial annual reports in India show no separate heading for hydatid disease, and in hospital reports they are included under tumours. It is therefore difficult to arrive at an estimate of the real prevalence of the disease in India. The dog, the natural host of the *Ecchinococcus granulosus*, though present in numbers, is rarely the household pet and companion of man as in



Illustration showing the large cyst arising from the lower pole of the left kidney. A portion of the hydatid membrane can be seen projecting from a tear in the upper part of the cyst.

Europe and Australia. Amongst both Mohammedans and Hindus, owing to religious scruples, dogs are rarely allowed in-doors. This might be a possible explanation of the rarity of the disease here, but it is equally possible that, as the senior writer holds, the condition is frequently overlooked. This paper therefore is intended to emphasise the not uncommon occurrence of this condition in south India where the senior writer has met with seven cases in the course of the last eight years.

The only possible means of estimating the prevalence of this condition in south India, since hospital reports are so meagre in this respect, is by an analysis of the cases of proved hydatid disease that are reported as such by the pathological department of the Madras Medical College, which serves as a central laboratory to which most specimens from the district and mofussil hospitals are sent up for pathological examination. We have been able to analyse the number of cases of proved hydatid disease through the courtesy of Dr. A. Goyle, professor of pathology of the Madras Medical College, from the records of the last 10 years. No cases were reported in 1923, 1926, 1927 and 1929; the incidence in the other six years is as follows:—

Year	Number of cases	Site of cyst	District
1924	one	liver	Madras
1925	one	abdomen	Madras
1928	one	liver	Madras
1930	two	abdomen	Madras
		liver	Madras
1931	one	not known	Anantapur
1932	two	liver	Kurnool
		neck	Anantapur

It will be noticed that only eight cases have been reported for the whole of the presidency during the last ten years.

The cases reported below serve to show that the real incidence is more than is apparent from the above figures, if care is taken to look out for this condition. It is possible that many cases of obscure enlargement of the liver looked upon as abscess or gumma are really cases of hydatid disease. Some puzzling abdominal tumours may come under the same head. These cases also serve to show what varying clinical types are presented. Five of these cases occurred while the senior writer was out in the districts during a period of six years, and the other two were patients that came up to Madras and were admitted to the wards of the Government Royapuram Hospital for treatment.

Case 1. Cyst of the liver.—R., Hindu, aged 45 years, came up for treatment to the District Headquarters Hospital, Vellore, in 1923 for a cystic tumour of the liver. On operation it was found that the cyst extended down into the peritoneal cavity and had formed adhesions to the colon and small intestines. It was a unilocular hydatid. Adhesions rendered the removal of the tumour *en masse* impossible, so the cyst was opened, irrigated and touched with formalin; the patient recovered without any complications.

Case 2. Cyst of the breast simulating cystadenoma.—Mrs. K. P., a young married Hindu lady, aged 35, came up for treatment to the District Headquarters Hospital, Guntur, in July 1929 for a tumour of the breast of four months' duration. The tumour was of the size of an orange, cystic and slightly tender. No suspicion of hydatid disease was entertained, since cystadenoma of the breast with large cysts is quite a common condition. On operation, however, it was found to be a large hydatid with a well-developed thick ectocyst and a delicate endocyst, besides the fibro-fatty capsule outside the cyst. A number of daughter and grand-daughter cysts were found inside the primary cyst indicating an endogenous development.

Case 3. Cyst of the abdomen simulating ovarian cyst.—C., a young Hindu lady, aged 31, came to the Hospital for Women and Children, Vannarpet, Palamcottah, in August 1926, for a tumour of the abdomen of two years' duration. The patient was a multipara and had four children. There was a large cystic tumour in the abdominal cavity. On operation this was found to be a large hydatid arising from the omentum, adherent behind but freely movable in front. The cyst was multilocular having three septa and containing daughter and grand-daughter cysts. The cyst was marsupialized and the patient had an uneventful recovery.

Case 4. Cyst of the liver.—J. C., a young Indian Christian girl of 25 years, came to the same hospital at Vannarpet for cystic tumour of the liver, in March 1925. The cyst was of two years' duration and extended down into the abdominal cavity. On operation it was found to arise from the under surface of the liver and to extend down to Poupart's ligament, displacing the liver upwards and pressing on the diaphragm. There were numerous adhesions to the omentum and coils of the intestine. The liver substance was stretched out and atrophied. Small cysts indicating an exogenous development were found in the right lobe of the liver. The cyst itself was multilocular. The patient made an uneventful recovery after operation.

Case 5. Suppurating hydatid simulating subphrenic abscess.—In July 1927, in Madura, K. A., a young Chetty girl, aged 13, was seen by the senior writer in consultation, for a swelling in the region of the liver. There was a history of fever with rigors for one month, and the gradual formation of a swelling in the upper abdomen on the right side. The blood showed a leucocytosis. The clinical features were suggestive of subphrenic suppuration, and exploration and drainage were decided upon. The tumour was incised and pus, yellowish in colour with no fecal smell, was found. A large amount was evacuated, but the sinus persisted. Fifteen days after the operation, gentle pressure brought out two small daughter cysts. The incision was therefore enlarged, all the daughter cysts were removed, and the wall was touched with formalin. The wound healed without any further trouble.

Case 6. Multiple peritoneal cysts causing retention and extravasation of urine.—K., a Hindu, aged 46 years, was admitted to the Government Royapuram Hospital in September 1931 for extravasation and retention of urine. Rectal examination showed a lumpy growth in the sacral region which was irregular. Nothing could be made out through the anterior abdominal wall owing to rigidity. A sacral tumour causing pressure on the urethra was thought possible, but on exploration the whole pelvis was found filled with five or six cysts covered over by the omentum. These were removed *en masse*, and microscopical examination showed typical hydatid structures with hooklets.

Case 7. Hydatid cyst of the kidney.—Mrs. M. B., a Mohammedan lady, was admitted to the Government Royapuram Hospital in January 1932. She had come from Guntur district for treatment for a swelling in the left side of the abdomen of five years' duration. It had started as a small tender swelling in the left lumbosacral region and had gradually increased in size for the last five years, till it extended from very near the left costal margin to the iliac crest. There had been a low type of fever for some months. The patient was a multipara, had three children, two boys and one girl, and her menstrual history was regular. Her general health was good. On examination the tumour was found to be tense and cystic, and to occupy the whole of the left side of the abdomen with a small projection to the right side about one inch above the umbilicus. There was slight movement with respiration. The skin was freely movable and the tumour itself was slightly movable from side to side. The surface was irregular and appeared divided into three lobes. The differential leucocyte count showed marked lymphocytosis. Eosinophiles were only 3.5 per cent. There was no

albumin in the urine, and urinary symptoms were absent. On operation the tumour was found to be a large cyst arising from the lower pole of the left kidney. The descending colon was adherent to the left side. The cyst had pressed on the ureter below and caused a slight hydronephrosis. The cyst and the left kidney were removed and on examination all the three layers of the hydatid were made out. The outer was the fibro-fatty capsule of the kidney. The contents consisted of clear watery fluid. Microscopical examination of a scraping from the endocyst showed scolices and hooklets.

Comment.—The occurrence of hydatid cysts in the breast in case 2 is certainly unusual, and is a factor to be borne in mind in the diagnosis of cystic tumours of the breast. The development of multilocular cysts in cases 3 and 4 is not in agreement with the idea of a restricted geographical distribution; this is claimed to be different from that of ordinary unilocular cysts. On the other hand, these cases occurring in India suggest that the multilocular cyst is a mere variation in the development of the cyst, which might be partly due to a defective formation of the ectocyst allowing an extra-capsular budding. In case 6 the multiple peritoneal implantation cysts apparently arose from a primary cyst in the recto-vesical pouch. Retention of urine due to pressure of a cyst on the prostatic urethra has not been hitherto reported, and might puzzle the clinician if this condition is not borne in mind. The cyst of the kidney in case 7 offered great diagnostic difficulties since abdominal tumours in this situation show many variations from the common clinical types.

It is noteworthy that an examination of the blood in cases 6 and 7 did not reveal an eosinophilia. The eosinophilia of hydatid disease, while it may be well marked at the commencement, may gradually subside, probably because the mother membranes undergo degenerative changes. This fact should be borne in mind and the absence of eosinophilia should not be taken as a negative indication, especially in old cases.

In view of the recent work on Casoni's intradermal reaction for hydatid disease and the positive results in 90 per cent. of cases reported by Dew and Kellaway, it is worth while that this simple cuti-reaction be made use of in India in all obscure tumours and cysts that occur in and about the abdomen.

THE ZONDEK-ASCHHEIM TEST FOR PREGNANCY AS STUDIED IN 200 CASES*

By K. B. MUKERJEE, B.Sc., M.B., Ch.B. (Edin.),
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THE investigations of Zondek, Aschheim, and Popanicolau on the functions of certain of the glands of internal secretion are now so well known that they are even a subject of undergraduate physiology. These studies have inci-

dentally led on to a biological test of pregnancy, known as the Zondek-Aschheim (1928) reaction; it is with this test that this paper is concerned.

After I had carried out the original test on twenty cases I began to doubt if the test could have a wide application since the clinician has to wait for the report for five days—rather a long time when he is faced with a case of, say, tubal pregnancy.

The use of immature white mice has some practical disadvantages; the disadvantages are: (a) sex-differentiation—recognition of the sex of immature mice is by no means easy; (b) the animals have to be bred for quite a long time to obtain immature females of nearly the same age ready for the test; (c) these small animals do not tolerate injections of large quantities of fluids, and thus the speed of the test—a matter of importance in most cases in which we want to do the test—is sacrificed by the necessity for continuing the injections for 3 or 4 days.

For this and other reasons Reinhart and Scott (1931) and other workers have used the rabbit for pregnancy tests. It is not necessary to use immature female rabbits provided they are not pregnant, but for the sake of uniformity of results and in order to produce a maximal reaction it is better to use immature animals of nearly the same age, say, 2½ months old.

A catheter specimen of urine need not be used. It will be better however to use such specimens whenever possible. It is moreover desirable to know the drugs—such as alkaloids and the heavy metals—the patient might have been taking, and to test all specimens for albumin and micro-organisms. Sometimes I injected contaminated urines without any untoward effects, but more often the animals developed peritonitis within 12 hours. In cases of bacilluria I have found the procedure recommended by Stewart (1931) most helpful. This consists in shaking the urine with a little ether and allowing the ether to evaporate from the urine in the incubator. Then the sample is for all practical purposes sterile.

The intraperitoneal has certain advantages over the intravenous route, because large quantities of fluids are more easily introduced and because rabbits are very liable to die soon after intravenous injection of urine containing albumin—a substance we do not infrequently find in the urine of pregnant women. Some workers have advocated the intravenous injection of 5 c.cm. of urine on two consecutive days, but I gave one injection of 10 to 15 c.cm. intraperitoneally, in order to save time.

Finally, for suspected cases of chorionic epithelioma I used concentrated urine. As the anterior-pituitary hormone is thermolabile at 60°C. the best procedure is to evaporate the urine *in vacuo* at 45°C. With a good vacuum pressure 100 c.cm. of urine can be reduced to 10 c.cm. at this temperature in about two hours.

* Rearranged by the Editor.

It is not necessary to use concentrated urine for other cases—not even for anxious or nervous mothers in the earlier weeks of pregnancy—because the concentration of the anterior-pituitary hormone in the urine shoots up sharply to its maximum before the end of the first month of pregnancy, falling very slowly as months go on. Ordinarily my procedure is therefore to inject intraperitoneally two starved animals each with 10 to 15 c.cm. of the morning urine rendered sterile when required. (The urine can be kept for 48 hours in a refrigerator without any loss of its hormone content.) For about an hour the rabbits lie flat in the lateral position, but with absorption of the fluid from the serous membranes they recover.

The results.—The results of the test, as ascertained by the presence or absence of hæmorrhagic follicles, are obtained after 24 hours. One does not always find ovaries studded with such follicles; nor does it seem to me that the number of such follicles is related to the hormonal concentration of the urine injected. I have often noted rabbits of the same litter reacting differently to the same amount of urine of the same case. Even ovaries of the same animal reacted differently. With the same urine I have not however obtained a totally negative reaction in one animal and a definite positive reaction in another.

I have again cut serial sections, to search for atretic corpora lutea and microscopic hæmor-

under a magnifying lens is all that is necessary. In the first two months of pregnancy the effects of œstrin on the genital apparatus of the experimental animals are not marked, but later marked congestion and œdema are observed in the horns of the uterus, vagina, etc., along with the changes in the ovaries caused by the hormone of the anterior-pituitary body.

The cases

In this series of 200 cases, 40 were in the Eden Hospital, Calcutta. I must express my indebtedness to Lieut.-Colonel V. B. Green-Armytage, I.M.S., of that hospital, without whose guidance and constant encouragement I could not have investigated such a variety of cases as I have done.

In the interests of economy in space notes on these 200 cases have been omitted. The cases can be grouped in the following way.

Group I

Undoubted and uncomplicated pregnancy from 5th to 9th month.

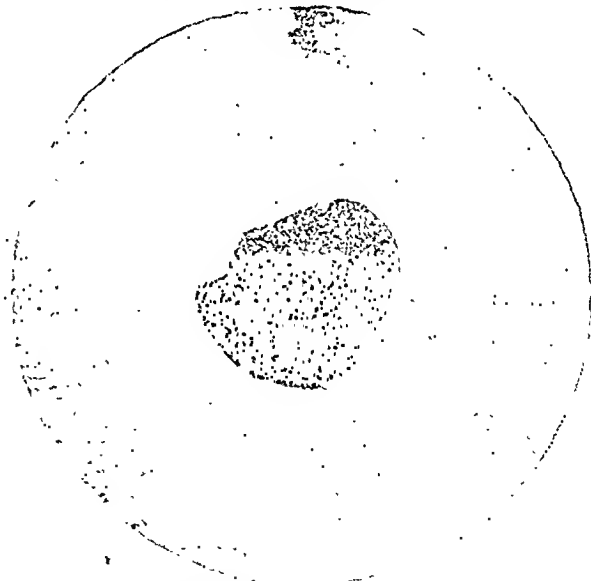
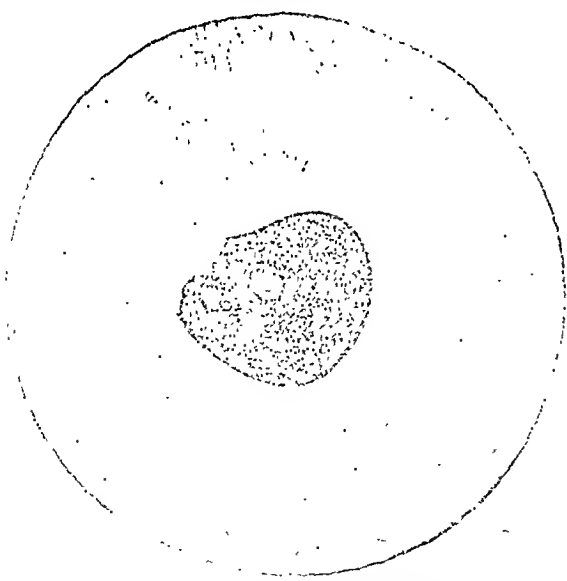
Nos. 1—17 (Private cases).

Nos. 18—27 (Hospital cases).

Results.—Zondek-Aschheim reaction positive in all cases.

Group II

Undoubted pregnancy but complicated with psychosis, pre-eclampsia, accidental hæmorrhage, hydramnios, malaria, kala-azar, syphilis,



The ovaries in positive cases are larger than those of control animals or in negative cases, and show hæmorrhagic follicles. The microscopic sections show much infiltration of blood into the Graafian follicles and the corpora lutea; they also show atretic corpora lutea.

Figs. 1 and 2. Case 137.—A case of chorionic epithelioma. Result obtained with concentrated urine is negative macroscopically and microscopically. Serial sections do not reveal any blood follicles and atretic corpora lutea.

rhages, of ovaries—'normal' to the naked eye—of animals injected with urines of suspected cases; but I have not yet discovered either of these conditions in a 'normal' ovary. For diagnosis a thorough inspection of the ovaries

filaria, 'anæmia', influenza, true diabetes, pulmonary tuberculosis, etc.

Nos. 28—50 (Private and hospital cases).

Results.—Zondek-Aschheim reaction positive in all cases except No. 48.

No. 48: Multipara, aged 28; pregnant 8 months; psychosis—extremely melancholic with revulsion of feeling towards the husband.

Labour complicated, breech presentation; Zondek-Aschheim reaction negative.

Group III

Cases with presumptive signs or symptoms of pregnancy, amenorrhœa ranging from 15 days to 8 months.

Nos. 51—85 (private and hospital cases).

Results.—Zondek-Aschheim reaction positive except in Nos. 57 and 82. With these two exceptions they all showed definite signs of

correct except on one occasion, the details of which are as follows:—

No. 137. Here the patient was admitted on August 22nd, 1931, with a history of abortion which, she said, had taken place on August 18th, 1931. Curetted products showed hydatidiform mole. Admitted for the second time on September 11th, 1931, with metrorrhagia. Relieved and discharged. Third admission on September 27th for vaginal bleeding. Pathological diagnosis of curetted products—chorionic epithelioma. The Zondek-Aschheim reaction with concentrated urine was negative. Blood transfused on September 30th, and on October 2nd vaginal hysterectomy, bilateral salpingectomy and right ovariectomy were performed. On October 19th the patient was discharged as cured.

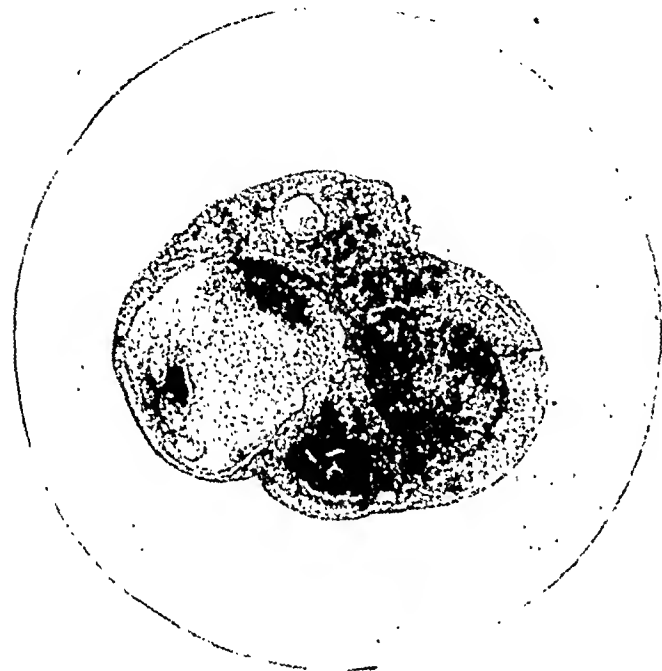


Fig. 3. Case 187.—A case of hydatidiform mole. Ovaries removed 24 hours after injection show both atretic corpora lutea and blood follicles.

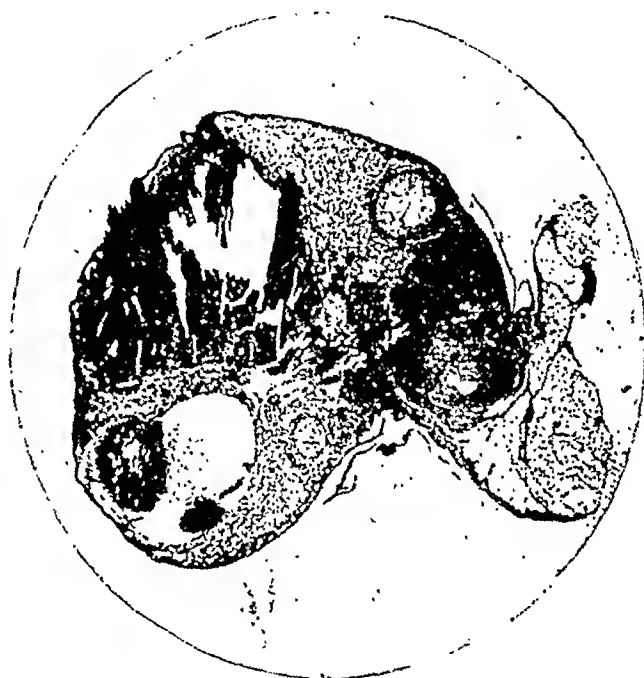


Fig. 4. Case 51.—A case of toxic hyperemesis, which was treated in the beginning as 'bilious attacks'. Twenty-four hours after injection the ovaries show the usual signs.

pregnancy in the later months, and the dates of labour closely agreed to their calculations.

No. 57: Nullipara, aged 42. Married 30 years; sterile. Amenorrhœa for 3 months when first seen. Zondek-Aschheim reaction negative. No signs of pregnancy when seen after six months of amenorrhœa. (? Psychological, ? menopausal.)

No. 82: Multipara, aged 42. Five children. Asthma with heart failure and anasarca; anæmia; amenorrhœa of 7 months; no vaginal finding except a small cervical polypus. Zondek-Aschheim reaction negative. The patient did not show any signs of pregnancy later. Anæmia might have caused the amenorrhœa.

Group IV

Cases simulating anomalous pregnancy.

Nos. 86—200 (Private and hospital cases).

In this group are included cases of threatened abortion, ovarian cyst, fibroid, fibroid and pregnancy, tubal pregnancy, salpingo-ovariitis, pyosalpinx, cystic ovary, hydatidiform mole, endometrioma, hæmatometra, etc.

Surgical measures in the cases of this group showed that the Zondek-Aschheim reaction was

No. 107, who was another case of hydatidiform mole, could not be followed up. When she left the hospital the Zondek-Aschheim reaction was totally negative.

Discussion

So far I have not got a single false positive reaction though I have examined over 200 cases and serially sectioned many ovaries that show no hæmorrhagic follicles to the naked eye.

It will probably be fallacious to argue that since we get so small a percentage of error—about 2 per cent.—we can safely rely on such a test. Judgement has to be made entirely from the point of view of the clinician. There can, for instance, be no comparison between an anxious mother, otherwise well, wishing to know if her month's amenorrhœa is due to pregnancy and a case where tubal pregnancy is suspected. In quite a number of cases of the latter type laparotomy is clearly indicated. Nevertheless, positive results are always reliable and sometimes valuable. Take case no. 100 for instance; the patient had a large sub-peritoneal fibroid

plus amenorrhœa of over six months' duration. Diagnosis of pregnancy was difficult for various reasons, and could not be made for nearly six days, but the Zondek-Aschheim reaction was positive straight away.

I am much indebted to Dr. R. M. Bradley, M.D., Ch.M., Medical Superintendent, B. I. S. N. Co., Calcutta, for kindly allowing me to perform most of these experiments in the Mackinnon, Mackenzie & Co.'s Clinical Laboratory, Calcutta, and to publish this paper. I would also take this opportunity of thanking most sincerely Lieut.-Colonel V. B. Green-Armytage, F.R.C.P., L.M.S., Professor of Obstet-

rics and Gynæcology, Calcutta Medical College, Dr. S. J. G. Nairn, M.B., F.R.C.S., of the Presidency General Hospital, Calcutta, Dr. B. K. Das, D.Sc., Formerly Professor of Zoology, Calcutta University, and Mr. N. G. Chakrabarti, M.Sc., Demonstrator of Chemistry, Presidency College, Calcutta, for the help and guidance they gave me.

REFERENCES

- Stewart, W. (1931). *Lancet*, Vol. I, p. 1347.
 Reinhart, H. L., and Scott, E. (1931). *Journ. Amer. Med. Assoc.*, Vol. XCVI, p. 1565.
 Zondek, B., and Aschheim, S. (1928). *Klein. Woch.*, Vol. VII, p. 1401 and p. 1453.

A Mirror of Hospital Practice

A RARE TYPE OF DERMAL LEISHMANIASIS

By E. MUIR, M.D., F.R.C.S. (Edin.)
and

S. N. CHATTERJEE, M.B., D.T.M. (Bengal)
Calcutta School of Tropical Medicine

Puzzling cases sometimes are sent to the leprosy outdoor clinic with a diagnosis of elephantiasis Græcorum which after a careful examination turn out to be cases other than leprosy. The undermentioned case is one of these.

The patient was diagnosed as a case of leprosy and referred by a doctor to the Albert Victor Hospital, Gobra, for admission. He was discharged after examination as he was not considered to be suffering from leprosy. Being disappointed he came back to the medical institute he attended on the first occasion. There

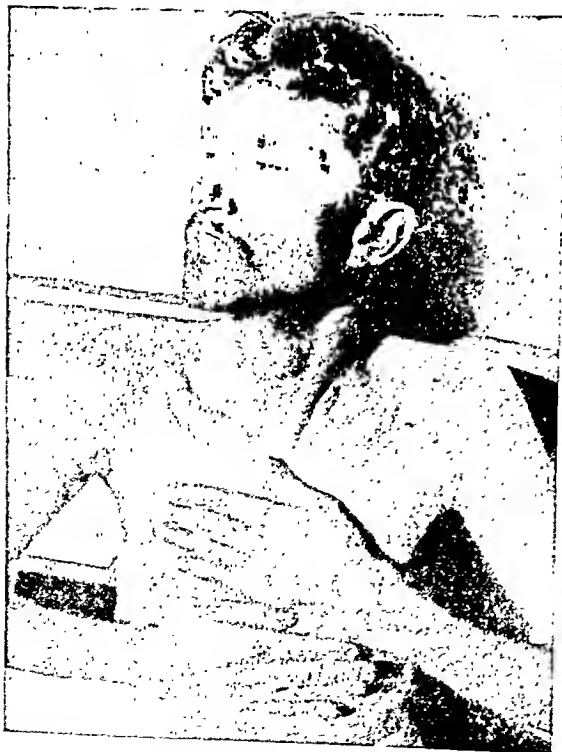


Fig. 1.—Front view of patient.

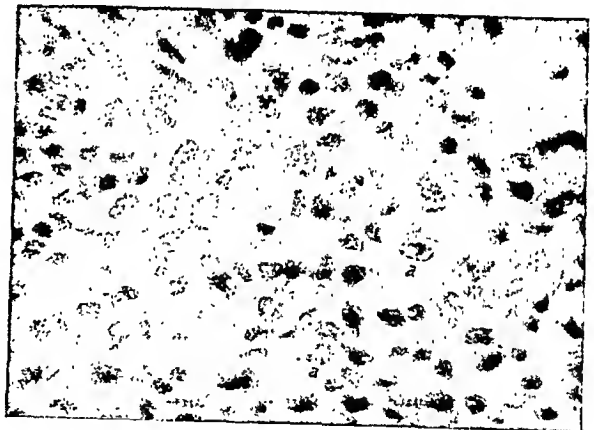


Fig. 2.—Photomicrograph of section taken from edge of annular lesion of arm. Note capillary surrounded by granulomatous cells, some (a) containing Leishman-Donovan bodies.

he was seen by another doctor who diagnosed the case as one of leprosy and referred him to the leprosy outdoor clinic of the Calcutta School of Tropical Medicine.

History and examination.—Seven years ago the patient suffered from an attack of 'fever' for about two months after which he noticed enlargement of the spleen. The spleen became normal in size without any special treatment. He noticed an erythematous thickened lesion on his abdomen about six years ago. The lesion gradually increased in size and became diffuse all over the abdomen, chest, back, neck and extremities. There were small nodules on the chin, lips and nose, and erythematous and annular lesions with thick crusts on the dorsum of the hands, forearms, feet, legs and knees. There was slight itching but no anaesthesia or deep analgesia. Pus was found on removing the crust of a lesion. Erythematous lesions were present on the glans penis and scrotum. The history of syphilis was negative. Most of the skin surface appeared dry, scaly and erythematous, but this condition was notably absent where the cloth was tied tightly round the waist. The

appearance is best understood from the accompanying illustrations.

Differential diagnosis.—There was a suspicion of syphilis owing to the presence of annular lesions, but

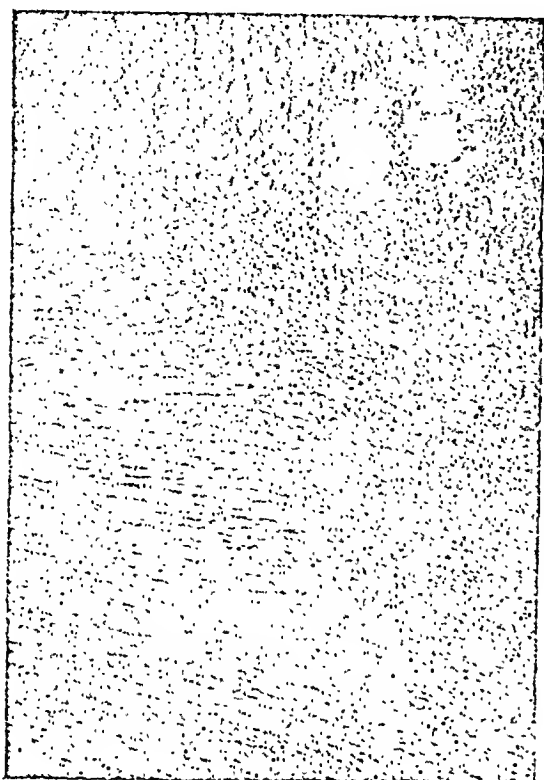


Fig. 3.—Skin of back of neck. A smear from the skin removed showed abundant Leishman-Donovan bodies.

that was ruled out as both the Wassermann and Kahn reactions were negative. Blastomyces was suggested, but the result of the examination by Dr. K. Banerjee, of the skin department, showed that there were neither fungi nor blastomyces. We took a smear from a lesion on the nape of the neck and from the annular lesions on the left ankle, left knee and left hand. Slides stained by the Ziehl-Neelsen method showed no acid-fast bacilli

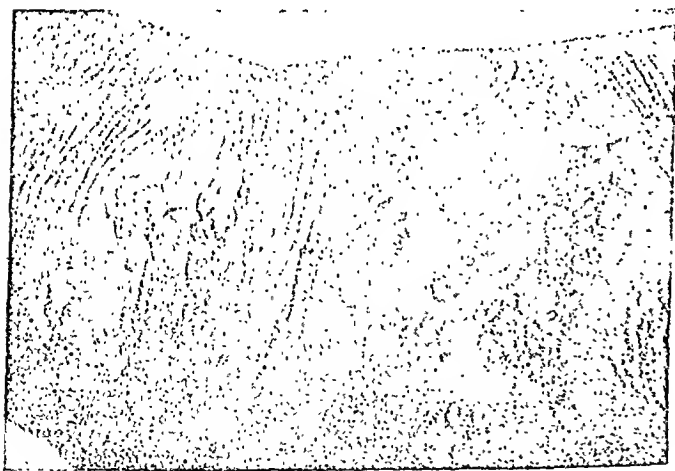


Fig. 4.—Back of hand showing annular lesions.

but those stained with Leishman's and Giemsa's stains showed numerous *Leishmania donovani* and cocci, especially, diplococci.

The special points of interest in this case are the persistent diagnosis of leprosy, the annular lesions which are uncommon in dermal leishmaniasis, and the accompanying dermatitis. As we have mentioned above, this

dermatitis was absent where the skin was protected by the cloth tied tightly round the waist; it may therefore have been due to intolerance of the sun's rays.

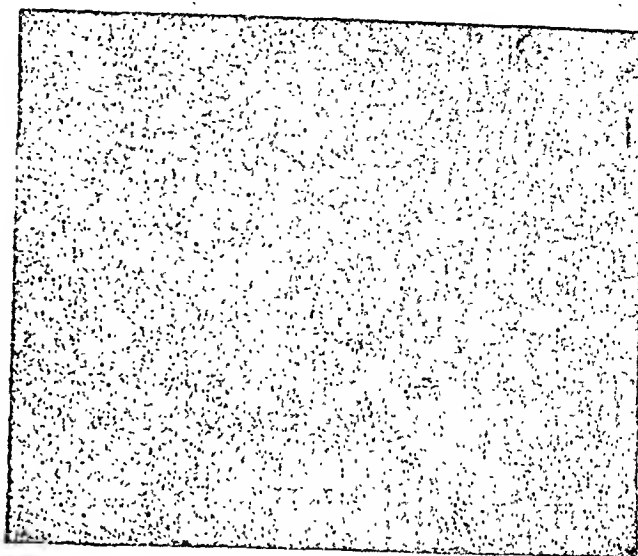


Fig. 5.—Skin of chest magnified.

Our thanks are due to Dr. K. Banerjee for kindly doing the bacteriological examinations.

A LEECH IN THE NASAL CAVITY AND ITS REMOVAL

By D. R. KAPUR, L.M.S.

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IN the year 1925 at Kishtwar, a lad about 18 years of age came to the hospital with the history that he had a leech in the right nostril. On examination nothing could be detected. A saline douche was ordered to be given through the left nostril with the direction that the patient should breathe with his mouth wide open. One pint of saline was thus used but with no result. Later the compounder suggested the indigenous method. A bowl full of water was brought and placed just below the right nostril. After three or four minutes the leech came down but it slipped back when being caught with a dissecting forceps. The bowl was again placed there and as soon as the leech appeared it was caught with a Spencer Wells forceps.

A CASE OF RABIES WITH AN UNUSUAL- LY LONG INCUBATION PERIOD

By S. S. HAJARE, M.B., B.S.

Good-Fellow Hospital, Palampur (N. G.)

A. P., a MAHOMMEDAN FEMALE, aged about 30 years, was bitten by a rabid dog on her right leg on 2nd September, 1931. She arrived at this hospital on the same day and the wound was carbolicised and dressed. She was sent to Ahmedabad Civil Hospital, the nearest centre for anti-rabic treatment. The patient before reaching the hospital at Ahmedabad had a fit which presumably was hysterical. This fit was translated by her attendants as the development of hydrophobia and so without taking any anti-rabic treatment the patient was brought back to her village. Thereafter she did not have any illness worthy of note and the wound of the dog bite completely healed.

On 10th November, 1932, she developed typical symptoms of hydrophobia and died on 12th November, 1932, after an illness of two days.

The interesting feature of this case is that the patient developed hydrophobia as much as 14 months after she was bitten by the rabid dog.

ACUTE INVERSION OF THE UTERUS*

By J. C. BHATTACHARJEE, L.M.P.
Sycotta Factory Hospital, Kharikatin, Assam

A COOLIE woman, Tanti by caste, aged 30 years, was admitted to the hospital at 4 p.m., on 14th October, 1932.

History.—The patient had just been delivered of her second child; the first child, now three years of age, was delivered naturally.

In the present case labour was short and delivery of the child successful. As the placenta did not come away at once the *dai* and others applied pressure over the abdomen, when they noticed a large mass protruding from the vulva.

On admission the patient was prostrated, with a pulse of 120 per minute, and temperature 97°F.

Examination.—The uterus was absent from its usual site and there was a hollow in the supra-pubic region.

A dirty mass, to which the placenta was partially attached, was found protruding through the vulva. It had a hard but elastic feel and there was not much bleeding. The vaginal mucous membrane was found to be continuous with the covering of the projecting tumour, the line of inversion being above the level of the cervix.

Treatment.—The protruding lump including the placenta was cleansed and bathed in hot lysol lotion. Then the placenta was peeled off gently. The inverted inner surface of the fundus was in partial view and was found to be ragged. Taxis was attempted, and after considerable difficulty, on account of uterine contractions occurring, the organ was successfully reduced. An intra-uterine lysol douche was given and the patient was also given an injection of ten cubic centimetres of puerperal antistreptococcal serum, with ergot and quinine by the mouth.

Puerperium.—The patient developed a mild degree of sepsis, running an intermittent temperature from normal to 101°F. from the next day, and the lochia were at first sanguineous and offensive but gradually became normal. She was given hot vaginal douches daily and every other day ten cubic centimetres of two per cent. acriflavine solution intravenously for four injections. She became completely afebrile from the 23rd October, and was discharged from the hospital on 26th October, 1932.

My thanks are due to Dr. D. Manson, M.B., Ch.B., Chief Medical Officer of the Jorehaut Tea Company, for his advice and his kind permission to send this note for publication.

A CASE OF TYPHOID FEVER WITH CEREBRAL SYMPTOMS

By A. R. MANSOOR, M.D. (Durh.),
D.P.H. (Eng. et. Edin.)

University Hospital, Aligarh

T. H., a male student, aged 17, was admitted into the University Hospital on the afternoon of the 26th of November, 1932.

Present history.—Complains of fever, cough, headache, backache and pain in the throat. Temperature 102.8°F., pulse 100, respiration 28, skin dry, tongue furred, throat congested, heart, lungs, liver, spleen and urine, show no abnormality, blood negative for malaria and other parasites, and shows no difference in corpuscular contents.

Previous history.—Had fever with rigors on the morning of the 25th, he had had no other illness since May 1932 when he suffered from malaria. Right up to the 25th he had been feeling absolutely fit, had had an ordinary motion on the previous day but none on the day of admission.

Treatment.—Calomel grs. 2 and sodium bicarbonate grs. 10 were given at night followed by saline in the morning. On the 27th and 28th diaphoretic and expectorant sedative mixtures were given. On the 29th he passed 10 motions, watery, yellowish, containing pieces of orange and a few shreds of mucus; on microscopical examination only a few *Entamoeba coli* were seen. Blood repeatedly negative for the last five days. Patient put on chlorine mixture.

On the 30th patient was restless, could not express himself, and there were sordes on the lips. In the afternoon he developed stupor and delirium. Blood taken in broth and bile media for culture. Given glucose and sodium bicarbonate by the mouth every 2 hours. In the evening the patient lost control over his anal and vesical sphincters. Bouts of delirium and stupor progressive.

1st December, 1932. Patient semi-conscious, refuses all nourishment, passing faeces and urine into bed. Intravenous saline 10 ounces given at 10 A.M. and then repeated at 12 noon. At 2-45 P.M. he felt intensely cold, had rigors and general cyanosis, pulse nearly imperceptible. Subcutaneous injection of digitaline and strychnine given.

2nd December, 1932. Stupor very slightly less; delirium the same, passed 8 motions into the bed, hot packs applied and 10 ounces of saline given intravenously. At 6 P.M. 2 pints saline administered per rectum. At 9 P.M. showed signs of consciousness, complained of pain on sites of injection, had violent fits of shouting, crying and restlessness which lasted throughout the night. Glucose and sodium bicarbonate repeated every 2 hours.

3rd December, 1932. Slight improvement, occasional glimpses of consciousness, wants tea, shouting and restlessness the same. Saline per rectum twice a day continued.

6th December, 1932. Condition after steady improvement for the last three days has retrogressed, toxæmia intense. Saline per rectum continued.

7th December, 1932. Toxæmia state practically over, definite improvement in the mental condition.

8th December, 1932. Pure culture of *Bacillus typhosus* isolated from the blood.

16th December, 1932. Steady improvement during the previous week, the patient recovered control over his sphincters for the first time.

17th December, 1932. A crop of blisters appeared over the front of the neck and over the front of chest and a few over the abdomen; culture from blisters taken. After 48 hours' incubation the culture medium was found to be sterile. On the 20th all blisters dried up leaving a fine powdery desquamation.

The temperature commenced to decline permanently towards the normal from the 24th, convalescence commenced from the 6th of January, and the patient was discharged as cured on the 11th.

A CASE OF NEURASTHENIA APPARENTLY CURED BY A DIET OF GHEE*

By R. K. BASU, L.M.S. (Cal.)

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A HINDU Brahmin, a lawyer by profession, aged 70 years, noticed the onset of the following symptoms in July 1930.

Both his mental and physical vigour gradually deteriorated until he finally lost all interest in life, both in his work and pleasure.

His appetite was poor and he suffered from obstinate constipation, but apart from these symptoms no physical cause for his condition could be discovered in spite of examination by numerous doctors.

As he was not improving he finally consented, on the advice of friends, to consult a Kaviraj practitioner in Calcutta. The patient did not go to see the practitioner but sent a detailed written history of his case and after

* Rearranged by the Editor.

* Abstracted by Editor.

study of this a small white powder was prescribed which had to be mixed with two drops of good ghee and taken every morning. In addition the patient was ordered to take at least one ounce of good ghee with rice both morning and night, and was told that all his vegetable curries must also be prepared with ghee.

These instructions were closely followed and the patient gradually increased the amount of ghee until he was taking about two ounces with each meal by the end of a fortnight. He now began to feel distinctly better and within two months he had gained ten pounds in weight and felt normal in every way.

Later, the amount of ghee was further increased until he was eating and enjoying three to four ounces with each meal. When I saw him nearly two years afterwards he was vigorous both mentally and physically and apparently completely restored to health.

This man was a highly emotional individual and I am of the opinion that mental disturbances had an effect on his endocrine system in some way, which upset his metabolism and the diet of ghee apparently restored this upset balance.

This case is of considerable interest in that it shows how important a part diet may play in effecting a cure. This is an aspect often ignored by some allopathic physicians who are inclined to rely too much on drugs alone.

In India the question of obtaining a diet sufficiently rich in vitamins is of extreme importance and I feel sure that great improvement in the general well-being of the people would be brought about if doctors were to pay more heed to diet and to learn which easily available articles of food contained the needed accessory factors.

CHORIO-EPITHELIOMA OR DECIDUOMA MALIGNUM

By J. M. DAS, L.M.S.

Teacher of Midwifery, Campbell Medical School, Calcutta

In my gynaecological and obstetrical practice I have seen and dealt with many cases of vesicular mole (hydatidiform degeneration of the chorion). Out of these I have seen four cases of a malignant nature—they are known as perforating or malignant hydatidiform mole or chorio-epithelioma and are sometimes called deciduoma malignum though it is a misnomer.

1st case.—In the year 1910 Lieutenant-Colonel C. R. McQueen, I.M.S., while Surgeon Superintendent of the Eden Hospital diagnosed a case of multiple fibroid, and when he opened the abdomen a branching brush-like growth was found perforating the uterus. He had to do total hysterectomy. I assisted at the operation.

2nd case.—About six years ago an Anglo-Indian patient was admitted in my ward in the Campbell Hospital and diagnosed as a case of vesicular mole, and I evacuated the uterus by dilatation and evacuation with a blunt flushing curette. She was discharged from my ward. In a month's time she came back, having irregular hæmorrhages and I curetted her and the scrapings were microscopically examined but there was no sign of chorionic cells or malignant proliferation. She was discharged after a month and a half, and subsequently admitted to the Eden Hospital where Lieutenant-Colonel Leicester, I.M.S., curetted her twice

and eventually had to do total hysterectomy as the bleeding continued. The specimen which is at the Eden Hospital shows a nodular growth on the fundus of the uterus.

3rd case.—About five years ago a patient was sent from the out-patient department having bleeding after a miscarriage of two months, in her home. She said she had passed many cauliflower-like growths and eventually the uterus became small but the bleeding continued. I scraped the uterus. The scrapings were examined and reported as chorio-epithelioma. I attempted vaginal hysterectomy but at the slightest touch of the knife she bled very freely. I sent her for radium treatment and after deep x-ray and radium needles insertion she was examined by me and I found her cured, leaving only scar tissue. The bladder was not affected. She is still under the observation of the radiologist and there is no sign of recurrence.

4th case.—This specimen I have demonstrated before the members of the British Medical Association (Bengal Branch). I removed it on the 7th of December 1932.

Patient, a Bengali, primipara, aged 25, admitted on the 18th of August. History of three months' amenorrhœa but the size of the tumour is about six months' pregnant uterus.

The case was diagnosed as vesicular mole and the following is the case history.

Admission—18th August, 1932.

30th August, 1932. (1) Evacuation of the uterus for vesicular mole—blunt flushing curettage; a large bucket full of the typical growth came out.

21st September, 1932. (2) Curettage again as the patient was bleeding off and on since the first evacuation.

27th September, 1932. (3) Examination—(a) Slight blood discharge. (b) Cystic mass on the left side.

It was diagnosed as chorio-epithelioma with cystic left ovary. As the patient was very weak with continuous malaise and slight fever, an operation was impossible and the general condition had to be improved.

7th December, 1932. Patient was operated on and total hysterectomy was performed and a cystic left ovary removed. The uterus which was bulky and retroverted contained a typical mass of chorio-epithelioma growth.

This case illustrates the importance of keeping vesicular mole cases under observation.

Special Article

NOTES ON INDIAN PLAGUE RATS

By W. J. WEBSTER, M.C.

MAJOR, I.M.S.

In the literature on plague there are several examples of the same rodent being referred to under different names. Changes in scientific names are of course unavoidable with advances in classification and adherence to the law of priority. A certain amount of information on the classification of rodents should be familiar to health officers and others who have to deal with plague outbreaks. It has been considered desirable to collect the essentials in this paper as they are not available without considerable study of the literature.

The nomenclature of certain rodents

The generic name 'Mus' used by Linnaeus (1758) applied not only to rats and mice but covered a multitude of rodents including guinea-pigs. The long-tailed house rat was then

known as *Mus rattus*. Trouessart (1881) introduced the name *Epimys* for rats and *Mus* was restricted to mice. Hollister (1916) noted that *Rattus* (Fitzing, 1867) had priority over *Epimys*, and the former has since been further referred back to Fischer, 1803. *Rattus rattus*, L., is therefore, the accepted name among English-speaking naturalists. *Mus rattus* is, however, still used by Italian writers and *Epimys rattus* continues to be recognised by French naturalists.

The sewer or ship rat was formerly known as *Mus decumanus* (Pallas, 1778) and was later referred to as *Epimys decumanus* or *E. norvegicus*. The correct designation at present is *Rattus norvegicus* (Erxleben, 1777). The other names may be encountered in current continental literature.

The so-called 'black' rat (*Rattus rattus*) may be brown and the 'brown' rat (*Rattus norvegicus*) may be black, and either may be grey. The description 'brown' has been applied to both and in Holland *norvegicus* has been called 'blue' (Jorge, 1928). These descriptions should be completely abandoned.

The name 'Mus' has been further restricted to house mice proper by the reintroduction of the genus *Leggadina* for field mice (Thomas, 1919). *Mus dubius* should now be named *Mus urbanus* (Wroughton and Davidson, 1920).

Blanford (1888) included bandicoots and mole rats under the generic name *Nesokia* or *Nesocia*. Thomas (1907) restricted *Nesokia* to the short-tailed mole rats of northern India. He introduced the name *Gunomys* to distinguish the long-tailed southern mole rats and revived the name *Bandicota*. Hence the confusion regarding *Nesokia bengalensis*. According to Wroughton (1908) the spelling *Nesocia* used by Blanford was without authority.

The identification of certain rodents

Rattus rattus belongs to the Order—Rodentia, Sub-order—Simplicidentata, Family—Muridae, Sub-family—Murinae and Genus—*Rattus*.

The Order Rodentia is distinguished from all other placental mammals by the two chisel-like central incisor teeth in each jaw. In the Sub-order Simplicidentata there is only one pair of upper incisor teeth while the Duplicidentata (hares and rabbits) have two pairs.

Muridae have only sixteen teeth, viz, two incisors and six molars in each jaw (formula 1003). About one thousand and three hundred species and varieties of Muridae have been described. The Family Muridae has to be distinguished—in India—from the squirrel family and the bamboo-rat family. Squirrels can be distinguished in doubtful cases by the presence of pre-molar teeth and the fact that the tibia and fibula are separate. Bamboo rats have very small ears and eyes and the limbs and tails are short. They are found in Burma, Assam and the Himalayas. The fourth family, the porcupines (Hystriidae), is easily recognised.

Murinae have sparsely-haired tails longer than half the head and body together, and the worn teeth show bands, either straight or curved, running transversely across the biting surface. Murinae have to be distinguished from members of the Gerbillinae sub-family which have a long hairy tail, usually tasselled, and from the Cricetinae (hamsters) which have a very short tail, less than half the length of the head and body together, and which in the Indian area are confined to high altitudes in the north.

To put it very briefly, the teeth of rats and mice number sixteen including chisel-shaped incisors, while the tail is practically hairless and longer than half the head and body together. Attention to these points would prevent confusion with animals having an outward resemblance to rats and mice, such as musk rats of the Order Insectivora and mongooses of the Order Carnivora.

Keys to twenty-three genera of the Murinae and to the species of these genera are given in the summary of the Indian Mammal Survey by Wroughton (1919). He gives twenty-one species of *Rattus* but apart from *Rattus rattus* the only species likely to be met with in the plains is *R. blanfordi* with the distal part of the tail white and with only six teeth. Hinton (1918) describes twenty-two members or sub-species of the *Rattus rattus* group.

Most places in India provide at least two members of the *R. rattus* group. In Bombay, for example, it is easy to select black or white-bellied or brown varieties but some specimens appear to be intermediate between these. Even if it were practicable in plague work, there is

			Length of head and body in inches	Length of tail as percentage of head and body length	Number of teeth	Characteristic noise
<i>R. rattus</i>	6-8	about 125 (100-150)	10-12	a series of squeaks
<i>R. norvegicus</i>	about 10	about 90	12	a prolonged squeal
Bandicota	over 9	about 90	12	a snarl
<i>Gunomys</i>	less than 9	more than 66	(may be 10)	a grunt
<i>Nesokia</i>	less than 9	less than 66	16-18 8	..

probably no advantage in distinguishing the sub-species. For practical purposes the colour may be ignored.

In the important genera *Rattus*, *Bandicota*, *Gunomys* and *Nesokia*, the anterior upper molar tooth measures not more than half the tooth row. In the genus *Rattus* the worn areas on the molar teeth are distinctly curved while in the other three genera mentioned these laminae are practically straight.

Some of the points useful in identification are given in the table. Other characters are:—

(a) *R. rattus*—tail of uniform colour showing about two hundred and fifty rings and a tiny tuft of hairs at the tip; ears and eyes large; top of skull shows an area shaped like a tennis racquet, the temporal ridges being convex outward. (b) *R. norvegicus*—tail often lighter below with about two hundred and ten rings less well marked than in *rattus* and a tiny tuft of hair at the tip; eyes and ears small; temporal ridges almost straight and parallel; soles of feet usually pinkish. (c) *Bandicota*—tail thick and blunt and shows rings; head narrow; long spinous hair all over body. (d) *Gunomys*—tail rather like that of *rattus* but rings less well marked and no tuft of hair at tip; spinous hair on back; head broad; palatal foramen long (about 8 mm.). (e) *Nesokia*—head broad; palatal foramen short (about 5 mm.).

Some of the other genera may be dismissed briefly. In mice of the genera *Mus*, *Leggada* and *Leggadilla* the anterior upper molar tooth measures more than half the tooth row. *Leggadilla* has well-marked frontal ridges while *Mus* and *Leggada* have none. The frontal ridges can be palpated through the skin on top of the head; they diverge backwards from just behind the eyes. *Leggada* is a jungle genus with a longer muzzle than *Mus*. The metads (genus *Millardia*) have less than six plantar pads. Bush rats of the genus *Golunda* have grooved incisor teeth. In the genus *Vandelluria* there is a flat nail, instead of a claw, on the first and fifth digits of all four feet.

The other thirteen genera are not widely distributed and are mostly confined to further India and the Himalayas. For the identification of these genera the tables quoted must be consulted. In some cases the location of the capture is a guide to the specific name. In many cases distinction depends on variations in colour which are not easily appreciated without specimens for comparison. The real colour is, of course, seen only in fresh specimens, and should be noted before preservation. Methods of measuring, skinning and preserving small mammals are given in a pamphlet entitled 'Instructions for Collectors: No. 1—Mammals' issued by the British Museum (Natural History).

Rattus norvegicus

Wroughton (1919) states that there is no authentic record of the taking of *norvegicus*

in India outside the docks of seaside towns. As *norvegicus* is common in Bombay where most of the investigations of the plague commission were carried out, somewhat undue stress has been laid on the importance of this species in Indian plague. Patton (1931) states that chronic plague persists in *norvegicus* in Bombay as in most parts of India (the italics are mine), and proceeds to explain that the epizootic begins in the young *norvegicus* population. Owing to the strictly limited distribution of *norvegicus* this explanation is misleading. As a result of the supposed importance of this species, those who have had occasion to examine rats in India have been too anxious to identify *norvegicus* and I know of several instances where the name was wrongly applied. One rat known only in Nepal has a superficial resemblance to *norvegicus* but is now named *Rattus rattus brunneus* (Hinton and Fry, 1923).

Plague rodents in public health work

As a result of its numerical density, wide distribution and domestic habits, coupled with its specific flea infestation *Rattus rattus* is by far the most important species of rat as far as plague in India is concerned. *R. norvegicus* is certainly of importance in Bombay. In Calcutta which has scarcely suffered from plague (perhaps because the rat flea index there is very low and mainly due to *astia*) *norvegicus* formed 88 per cent. of the rats examined in connection with the recent survey (Strickland and Roy, 1930). These two species should be identified definitely. Examples of *Bandicota*, *Gunomys* and *Nesokia* should at least be recognised as such, to avoid confusion with *rattus* and *norvegicus*. Other rodents should be identified if possible when plague infected or when they harbour unrecognised fleas. Plague infection of rodents other than the Murinae (e.g., hares and squirrels) and in fact of mammals other than rodents may occasionally be met with. This, however, appears to be much less important in India than in other plague-infected countries.

REFERENCES

- Blanford, W. T. (1888). *Fauna of British India, Mammals*.
 Hinton, M. A. C. (1918). *Journ. Bombay Nat. Hist. Soc.*, Vol. XXVI, p. 59.
 Hinton, M. A. C., and Fry, T. B. (1923). *Ibid.*, Vol. XXIX, p. 399.
 Jorge (1928). *Les Faunes Regionales des Rongeurs*. Paris: Masson et Cie.
 Patton, W. S. (1931). *Insects, Ticks, Mites and Venomous Animals*, Part II, p. 255. Liverpool School of Tropical Medicine.
 Strickland, C., and Roy, D. N. (1930). *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXIII, p. 497.
 Thomas, O. (1919). *Journ. Bombay Nat. Hist. Soc.*, Vol. XXVI, p. 417.
 Wroughton, R. C. (1908). *Ibid.*, Vol. XVIII, p. 736.
 Wroughton, R. C. (1919). *Ibid.*, Vol. XXVI, p. 776.
 Wroughton, R. C., and Davidson, W. M. (1920). *Ibid.*, Vol. XXVI, p. 1025.

Indian Medical Gazette

APRIL

THE CLASSIFICATION OF THE ANÆMIAS

A MEDICAL man returning to civilization after an absence of 15 years would receive many shocks; not the least amongst these would be when he encountered an article in a recent medical journal on some disease associated with anæmia. He would naturally find that he was a little out of date and would turn with confidence to a recent edition of some standard textbook on medicine, and then his real trouble would begin. He would encounter the familiar opening, 'Anæmias can be divided into two groups, primary and secondary; the primary anæmias are chlorosis and pernicious anæmia; secondary anæmias do not arise spontaneously, but are the result of other pathological processes, etc.'. He would read on and find that little was said about chlorosis, except that the disease had practically disappeared, and that so much is now known about the 'other pathological processes' that result in pernicious anæmia that he would wonder why the definition of a secondary anæmia could not be applied to it; he would read still further and find that despite the great advance that had been made in our knowledge of anæmias there was still considerable doubt as to the nature of the 'other pathological processes' to which some of the secondary anæmias were secondary. In a state of mental confusion he would put the book down and would ask himself why the writer of the textbook had not had the courage of his obvious convictions and given a new classification of the anæmias.

The answer to this question is evident; during the last few years the inadequacy of the old classification has been fully realized and every hæmatologist has attempted to supply a new one, but no classification has yet been suggested that will satisfy the majority. Consequently, writers of textbooks that are primarily for the use of the undergraduate student will not take the responsibility of adopting any one of these new classifications; they fall back on the old one and try to make the best of it.

It cannot be said that any great advances have been made in the technical side of hæmatology during the last few years—especially if we exclude the intra- and supra-vital staining methods which are applicable mainly to the leucocytes—but new emphases have been applied to different aspects of the subject; for example, the hæmatocrit is not a new instrument and red blood cells have been measured from the time of van Leeuwenhoek,

but the emphasis which has been laid by recent workers not only on the mean size of red blood corpuscles but also on the dispersion round that mean has led to a very distinct advance in our understanding of certain anæmic states.

One of the newer methods of classification is according to the size of the red cell; we have macrocytic anæmia—of which the typical example is pernicious anæmia, normocytic anæmia—which includes true secondary anæmia (that is anæmia following acute hæmorrhage) and certain aplastic anæmias, and microcytic anæmia; the last-named group is divided into simple microcytic—the orthochromic anæmia associated with chronic disease, and microcytic hypochromic, in which are included simple achlorhydric anæmia and the anæmia following chronic hæmorrhages. This classification has the advantage of extreme simplicity; it probably appeals to the medical student and to the amateur hæmatologist who, equipped with an halometer and a Talqvist scale, is now prepared to give an 'authoritative' opinion on any case of anæmia.

It is not however a very helpful classification as it gives no indication as to the ætiology of the various anæmias, and a classification is required which takes some account of the pathological processes which bring about the conditions. A very clear exposition of our present knowledge regarding anæmias was given by Dr. Witts in last year's Goulstonian lectures; the lecturer himself has contributed no small part to the recent advances in this subject. Though he has not supplied a summarized classification he has dealt with the subject from the ætiological aspect, and we feel that no classification which does not take this aspect into account will be satisfactory. The following, which is mainly based on the teaching contained in these lectures, is an example of such a classification:—

(a) *True secondary anæmia* due to loss of blood either from the skin, from mucous or from serous surfaces; this loss may be acute or chronic, and the anæmia is accordingly normocytic orthochromic or microcytic hypochromic.

(b) *Anæmia due to errors of erythropoiesis*; these may be due to:—

(i) Aplasia or hypoplasia of toxic or mechanical origin.

The anæmia here is caused by a functional failure of the bone marrow; it is normocytic and usually orthochromic. It may be brought about by long-continued septic processes, by chemical poisons such as arsphenamin, by exhaustion of the bone marrow as a terminal condition in other anæmias especially pernicious anæmia, or by displacement of the bone marrow by proliferation of non-erythrocytic tissues.

(ii) Dysplasia.

Under this heading are the deficiency anæmias, on which there has been so much important work done recently. The anæmia may be

macrocytic or microcytic according to whether the blood formation has been checked at the megaloblastic stage, as in pernicious anæmia and the specific anæmia of pregnancy by the absence of 'Castle's intrinsic factor' and vitamin B, respectively, or at the normoblastic stage, as for example in simple achlorhydric anæmia, the nutritional anæmia of infancy, and the anæmia of sprue, which are caused by deficiency of, or failure to absorb, iron, vitamin C, etc.

(c) *Anæmia due to errors of erythrolysis*; these can be divided into :—

(i) Anæmias due to defects in the red cells themselves; they may be of congenital origin, or caused by parasitization or hæmolytic poisons, either chemical or biological.

(ii) Anæmias due to hyperfunction of the tissues responsible for the disposal of obsolete red blood cells, the reticulo-endothelial cells in the spleen and elsewhere.

The nature of this anæmia will be influenced by a number of factors, according to whether the blood destruction is acute or chronic, and according to the way the bone marrow reacts. If there is a sudden destruction of red blood cells the reaction of the bone marrow may be so brisk that not only will there be large numbers of reticulocytes but there may also be macrocytes and even nucleated red cells in the peripheral blood; however, the usual blood picture is a normocytic orthochromic anæmia. Other changes which accompany increased blood

destruction will also vary according to the acuteness of the hæmolysis, from hæmoglobinuria and jaundice to simple urobilinuria.

It is true that there are anæmias which we have difficulty in placing in a classification like the above, but this is not the fault of the classification so much as of knowledge of the ætiology of the disease. As our knowledge advances there is no doubt that from time to time anæmias that have been classed in one group will be moved to another group; a recent example of this has been pernicious anæmia. For many years this disease has been considered to be a hæmolytic anæmia; we were misled by the presence of abnormal quantities of the products of hæmolysis, urobilin and stercobilin, in the urine and fæces. We now know that these were evidence not of increased blood destruction but of the inability of the organism to utilize again the normal products of hæmolysis, and that pernicious anæmia is due not to an error of erythrolysis, but to an error of erythrogenesis. If liver is given in a case of pernicious anæmia, erythrogenesis again proceeds normally and excessive bilirubin excretion ceases.

Rapid advances have been made in our knowledge of hæmatology during the last few years, and we feel that, for the sake of the rising generation of medical students as well as for their teachers and examiners, the time has now come when these advances should be consolidated by the adoption of some new standard classification for the anæmias.

Medical News

EXTRACTS FROM THE MINUTES OF A MEETING OF THE BENGAL COUNCIL OF MEDICAL REGISTRATION HELD ON THE 18TH AUGUST, 1932.

NOTIFICATIONS announcing the appointment of the undermentioned gentlemen as members of the Bengal Council of Medical Registration were recorded:—

Name	In place of
(a) Lieut.-Col. Sir Hasan Suhrawardy, Kt., I.T.F.	Dr. R. V. Clayton.
(b) Lieut.-Col. C. R. Rai Sahib O'Brien, I.M.S.	Dr. Satishchandra Ghosh, I.M.S.
(c) Major T. H. Thomas, I.M.S.	Major S. J. V. Fox, I.M.D.
(d) Lieut.-Col. T. C. Boyd, I.M.S.	Lieut.-Col. D. P. Goil, I.M.S.

Government letter conveying sanction to the levy of a charge of Rs. 5 for incidental expenses of this Council from practitioners registered in other provinces on their admission free of fee to the Bengal Medical Register was recorded.

Notification announcing the appointment of Dr. B. N. Ghosh, representative of the Bengal Council of Medical Registration and the Governing Body of the State Medical Faculty of Bengal as a member of the Sanitary Board, Bengal, was recorded.

The following two gentlemen being representatives of the Bengal Council of Medical Registration and the State Medical Faculty of Bengal were re-nominated as

members of the Bengal Sanitary Board for a fresh term:—

1. Dr. B. N. Ghosh, L.M.S., F.R.F.P. & S.
2. Dr. T. Ahmed, M.B., D.O.M.S., F.R.C.S.

Order of the Government of Bengal accepting the reciprocity of registration in Bengal, of practitioners registered in Madras was recorded.

The Council decided that all registered practitioners be informed that in the opinion of the Council certificates of death might legitimately be granted by registered practitioners only when they were actually present at the time of death of the patients or saw the deceased very soon after death.

Dr. Kedarnath Das, C.I.E., M.D., F.C.O.G., moved that the following institutions should be inspected before the next meeting of the Council:—

- (a) Dacca Medical School.
- (b) Mymensingh Medical School.
- (c) National Medical Institute.
- (d) Calcutta Medical School.
- (e) Jackson Medical School, Jalpaiguri.
- (f) Chittagong Medical School.

The motion was approved.

An application from the Superintendent, Bengal Medical Institution and Hospital, Beliaghata, praying that the institution be granted affiliation to train students for the licentiate examinations of the State Medical Faculty of Bengal was considered and the superintendent was requested to furnish particulars of the institution in the form of return prescribed by the Council.

The Council recorded reports of two prosecutions under Section 6 of the Indian Medical Degrees Act, 1916. The amount of fine imposed by the Court is noted against each name—

1. Manicklal Mukherjee—Sentenced by the Sub-Divisional Officer, Bongaon, to a fine of Rs. 35.
2. S. A. Rahman—Sentenced by the Magistrate of Scaldah, to a fine of Rs. 5.

THE GODAVARI DISTRICT MEDICAL ASSOCIATION, COCANADA. FIRST ANNIVERSARY CELEBRATION.

THE First Anniversary of the above Association was celebrated on the 18th February, in the premises of the M. S. N. Charities Buildings, Cocanada, under the presidency of Rao Bahadur Dr. T. S. Tirumurti of Vizagapatam. 85 members, including a number of lady doctors, and 23 non-member doctors attended the function from all over the district, including 3 from West Godavari. Major T. S. Shastry, I.M.S., was elected as president, Drs. Audinarayanaswami and Kamaraju as joint secretaries, and Dr. Miss T. K. Narayanaswami, Dr. S. Swami Naidu of Rajahmundry and Dr. B. S. S. Prasada Rao of Samalkot as members of the managing committee for the new year. Rao Bahadur Dr. T. S. Tirumurti, after expressing his great pleasure at the large attendance, delivered a very interesting and instructive lecture on 'Some Recent Advances in our Conceptions and Diagnosis of Disease'. Major Shastry then talked about the necessity of conducting a leprosy campaign in this district and exhorted all the members of the Association to co-operate in their respective areas when the campaign was organised; other members took part in the discussion.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of April, 1883, Vol. XVIII, pp. 104, 99 and 105)

THE observations and researches of Dr. Patrick Manson of Amoy, regarding the life history of *Filaria sanguinis hominis* and the pathology of the diseases associated with it, are well known. In a recent paper published in the *China Customs Gazette*, he addresses himself to the elucidation of the apparent paradox, that, while in the majority of cases in which the blood is found to be infested with embryo filariæ no pathological disturbance of any sort is discernible, in a certain

number phenomena indicative of impeded lymph flow through the glands exist. It is important to recollect that the parent worm inhabits the lymphatics on the distal side of the lymphatic glands, and that the embryos swarm into the blood by passing through these glands. Why is it that in most cases this migration is accomplished without irritation of either the glands or the lymphatic vessels (afferent) beyond them; while in a few much irritation of both is abundantly manifest, and gives rise to painful enlargement of the glands and dilatation of the vessels, with effusion of lymph on the surface or into the surrounding tissues, the result eventually being hyperplasia of the lymphatic area implicated? His explanation of the anomaly is, that normally the parent worm is viviparous, and ejects from its uterine sac embryos which have uncoiled themselves and stretched their investive chorionic envelope so as to form a closely fitting outer garment corresponding in shape to that of the embryo, and not impeding its movements; whereas in certain cases the parent worm aborts—is oviparous—and discharges circular ova in which the embryo remains coiled in the chorionic envelope which it is unable to stretch. The diameter of the circular ovum is greater than that of the filiform embryo ($\frac{1}{250}$ to $\frac{1}{500}$ against $\frac{1}{3,000}$); and no aid in propulsion is gained from the active movements of the latter.

* * *

Quinetum the well-known 'Cinchona febrifuge', it is to be remembered, represents the whole of the alkaloids of the *Cinchona succirubra* bark, the proportions being approximately as follows:—

Quinine	4½ to 6 per cent.
Cinchonidine	24 " 30 " "
Cinchonine	38 " 45 " "
Amorphous alkaloid	14 " 21 " "

* * *

The Surgeon-General, H. M.'s Forces in Bengal, has issued a warning to officers commanding regiments, that an epidemic of cholera is about to take flight from Bengal and wing its way up the Gangetic plain. Precise dates of its anticipated arrival at particular stations are given. We hope that this warning may prove to be a needless one. No harm can come of putting the authorities on the alert, but announcements of this kind should be cautiously made to avoid creating panic.

Current Topics

The Treatment of Some of the Commoner Skin Diseases

By R. M. B. MacKENNA, M.D. (Camb.),
M.R.C.P. (Lond.)

(Abstracted from the *Medical Press and Circular*,
December 14, 1932, p. 487)

IMPETIGO CONTAGIOSA

THE standard casualty department treatment for this is dilute nitrate of mercury ointment applied copiously. Impetigo is an acute infection of the skin with streptococci and/or staphylococci, and is characterised by the effusion of a copious sero-purulent exudation from the affected area. If the usual mercurial ointment is applied on lint, it forms a waterproof covering under which the exudation may spread, thus infecting adjacent areas. Further, the fatty base of the ointment retards the normal heat loss from the skin, the temperature of the covered area rises slightly, the openings of the sweat and sebaceous glands are dilated, and a very fertile soil is prepared in which the cocci may increase and multiply in warmth and comfort. Cases of impetigo caused by

relatively innocuous strains of bacteria may respond to the standard treatment with dilute nitrate of mercury ointment, but if the infecting organisms are of a virulent nature, or the resistance of the patient is low, the condition of the patient rapidly goes from bad to worse. Good results may be obtained by the following line of treatment:

- (1) Remove the crusts either by softening them with olive oil, or by the application, for six or eight hours, of a starch and boracic poultice.
- (2) Apply the following lotion six or eight times daily:

R̄ Sulphuri precipitati	..	gr. ii
Ichthyol	gr. iii
Calaminæ preparatæ	..	gr. lx
Zinci oxidi	gr. xxx
Glycerinæ	ʒ. x
Aquæ calcis	ʒiv
Aquam ad	ʒi
M.		

- (3) Remove the crusts regularly once every thirty-six hours.

(4) When the exudation ceases, and the only symptom is slight redness of the affected areas, apply the following ointment twice daily:

R Hydrargyri ammoniati .. gr. v
Paraffinum molle 5i

It will be seen that the rationale of this line of treatment is to soothe the inflamed areas with a modified calamine lotion, to increase the formation of crusts, so that the exudation is localised, and to apply the lotion so frequently that the ichthyol and sulphur, and to a lesser degree the other ingredients, can exert their antiseptic action on every drop of exudate. Cases which do not respond to this line of treatment frequently respond quickly if the following lotion is applied freely four times daily to the affected parts:—

R Hydrargyri perchloridi .. gr. 4
Spiriti methylati industrialis .. 5fs.
Glycerini m. v
Aquam ad 5i

Never forget the impetigo in children, commencing on the ears or in the scalp, is usually secondary to pediculosis capitis. If lice or nits are found, and the impetiginous eruption is at all widespread over the scalp, the best line of treatment is to cut the hair short, and apply compresses of perchloride of mercury lotion (*vide supra*) thrice daily to the scalp.

Furunculosis.—Furunculosis is a disease caused by cocci, and frequently is difficult to eradicate. We should remember that in all cases of boils the urine must be tested before treatment is commenced. Even if there is no sugar in the urine the patient will benefit if his intake of carbohydrates is halved, and spicy foods, should be taboo. There is one point with regard to furunculosis which is not usually emphasised, and that is that an attack of boils commonly develops after several months, or even years, of self-neglect, and unless the patient's life is regulated from all aspects, furunculosis frequently becomes distressingly chronic. The house surgeon, during the last weeks of his appointment; the student or the nurse working for his or her examinations; the school-mistress, towards the end of term; the adolescent struggling with higher school certificate, a mass of unresolved sex complexes, and the frequent over-strain of team games; the typist or clerk who is habitually constipated and never takes exercise; the workman who suffers from chronic under-nourishment, and lacks personal cleanliness—all these are types which often give a history that they started to have boils, and despite much treatment, the boils have continued to erupt—often in crops—from time to time. If the physician is content merely with the usual local and tonic treatment, the condition of the patient frequently goes from bad to worse. Frequently the patient herself is her worst enemy. The stenographer will indignantly state that she is getting at least an hour and a half exercise in the open air daily, looking after her bowels, and doing all things as she has been directed, and yet she is not better. She does not tell you that she smokes fifteen to twenty cigarettes a day, frequently takes aspirin in large doses, invariably reads in bed until one o'clock in the morning, and never sleeps with her window open. Similarly, the workman will conscientiously go to the local bath-house thrice a week, and even have potassium permanganate baths, but if we have forgotten to warn him that it is no use attempting to disinfect the skin in this way, when on leaving his bath he dons an old and unwashed woollen vest on which is the coagulated excretion from the half-dozen boils from which he has previously suffered, then he will continue to suffer from furunculosis. These matters seem so simple that they are seldom referred to; frequently, however, persons go on from month to month suffering from boils or carbuncles, and if the physician would only discuss fully his patient's habit of life, he would discover and be able to rectify apparently trivial matters which are frustrating the whole of his treatment.

The local treatment of furunculosis has been so thoroughly dealt with in various recent publications that I intend only to make brief reference to it here. The most modern line of treatment is by solutions containing antiviral, or jellies containing bacteriophage. For boils of the external auditory meatus, gauze plugs soaked in antiviral solution and changed three or four times daily are excellent, and I have had good results from packing the cavities of carbuncles with bacteriophage jelly; but for the average case of furunculosis it has been my experience that the benefit obtained by the use of polyvalent staphylococcal antiviral is in no way commensurate with the high cost of treatment. For the majority of cases I prefer to give non-specific therapy in the form of intramuscular injections (once weekly) of 1.5 c.c. butyrate of manganese, or collosol manganese in the increasing doses recommended by the makers; concurrently, most cases benefit if given two tablets of oxide of tin (stannoxyl) thrice daily before food, and a drachm of Easton's syrup (B.P., 1914) thrice daily after food. Many authorities prefer to use vaccines rather than the preparations of manganese; an auto-genous vaccine is frequently excellent; stock vaccines are successful in some cases.

Erysipelas.—One of the most dangerous diseases due to cocci is erysipelas; facial erysipelas frequently ends fatally. Recent work has indicated that injections of milk frequently benefit apparently hopeless cases. One such case particularly impressed me; the case was one of facial erysipelas following a graze on the bridge of the nose in a man of sixty years of age. Despite the subcutaneous injection of large quantities of both polyvalent anti-streptococcal serum and anti-scarlatina serum, the patient's temperature had for a week swung between 101° to 103°; both cheeks, eyelids, and the forehead were affected, and the spreading edge of the eruption was travelling rapidly over the scalp. At 1-30 p.m. on the seventh day of the illness, 10 c.c. of aolan (detoxicated milk protein—Beiersdorf) were injected intramuscularly. By 8 p.m. the patient's temperature had risen to 105°, but during the night the temperature dropped to normal, and although no further injections were given, the temperature did not again rise, and the eruption rapidly disappeared.

Fresh milk may be prepared for injection by boiling for four minutes, cooling to body temperature, and straining through sterile gauze. Sayed has had good results by the intramuscular injection of 10 c.c. of milk in cases of facial erysipelas, and also claims that 'intra-dermal injections of sterile milk made parallel to and about 1½ inches away from the spreading margin of erysipelas produce a local reaction which prevents further extension of the infection at the site of injection, and improves the condition elsewhere'.

Supplies of serum may be difficult to obtain in some country districts, but there is usually an adequate supply of fresh milk, and the practitioner faced with an acute case of erysipelas may find that even if he cannot manage an intra-dermal injection, an intramuscular injection of milk may influence very favourably a case which could otherwise give rise to much anxiety. If a case of erysipelas is going to respond to intramuscular injections of milk, usually only two or three injections are necessary, and many cases clear up after a single injection.

Sycosis.—Cases of coccogenic sycosis are frequently extremely resistant. Many cases will respond to the following line of treatment:

(1) Clean up the face carefully, puncturing any pustules, and expressing their contents. If a hair is visible at the centre of any pustule, remove it with a pair of forceps. Remove any crusts either by means of a starch and boracic poultice, or with olive oil.

(2) Instruct the patient to desist from shaving, but to keep the beard short by clipping or cutting with scissors.

(3) Fold some white gauze so as to make a pad about six layers in thickness, soak it well in the perchloride of mercury and spirit lotion (*vide supra*), and place this in close contact with the skin for half

an hour at a time, and instruct the patient to carry out this procedure thrice daily.

(4) Remove the gauze compress after the half-hour has elapsed, and apply either calamine lotion with 1 per cent. ichthyol, or the following ointment:

R̄ Hydrargyri ammoniati	..	gr. iv
Ichthyol	..	gr. iv
Paraffini mollis	..	ʒi

(5) If there is any blepharitis this must be treated on the usual lines, for the tear sac and the intra-nasal mucosa become infected with organisms washed off the eyelids by the tears, and the skin of the upper lip becomes constantly re-infected from these sources.

(6) General treatment includes avoidance of exposure to bright sunlight or cold winds; a wisely disciplined mode of life, tonics, and also a course of injections of butyrate of manganese.

If these measures fail, one may have recourse to such coal tar derivatives as acriflavine or brilliant green. Either may be used in an ointment (1 to 2 per cent.) or in a lotion (1 in 1,000). Some authorities recommend strongly alcoholic solutions of brilliant green. The following ointment, for the formula of which I am indebted to Dr. P. B. Mumford, occasionally cures cases of syccosis which have resisted other lines of treatment:

R̄ Sulphuri precipitati	..	ʒi
Balsami peruvani	..	ʒi
Unguenti diachyli	..	ʒi
Paraffini mollis	..	ʒii
M.		

Sig.—Apply twice daily.

If these measures fail, then the practitioner will probably have to refer his patient to a dermatologist, who will decide whether or not the case is one which will benefit from epilation with x-rays, or from some other treatment.

Adenoids

By F. PEARCE STURM, M.D., CH.M.

(Abstracted from the *Practitioner*, November, 1932, Vol. CXXIX, No. 5, p. 560)

Functions of the respiratory tonsil

For many years I have been engaged in a clinical and pathological research upon the problem of the adenoid child. The evidence so obtained is overwhelmingly in favour of the conception of the pharyngeal tonsil as a protective mechanism for the respiratory tract, but here there is space only for a summary of a few points.

(1) The respiratory tonsil or adenoid acts as a test organ for the respiratory fluids, namely, the inspired air and the systemic blood-current. It takes samples of all atmospheric micro-organisms and prepares immunizing substances from them.

(2) It is a probable survival of the oosphadium or test organ of water-breathing animals, and undergoes a functional hypertrophy when the respiratory and circulating currents are contaminated.

(3) This functional enlargement, though protective in intention, now causes obstructive and other difficulties for evolution has built a palate which divides the simple primitive mouth into an upper respiratory and a lower buccal compartment, and the respiratory tonsil is confined within the narrow, bony limits of the former.

(4) Hypertrophy of the respiratory tonsil, though not a disease, but a purely protective reaction, becomes pathological and calls for surgical removal when its presence in the narrow confines of the nasopharynx causes a greater disability (aural or respiratory) than is counterbalanced by the increased physiological activity which is the purpose and result of the hypertrophy.

(5) There is abundant evidence that leucocytes, laden with captured bacteria, come to the germ centres of the tonsil for destruction. This observation applies also to

the faucial tonsils and to the appendix, which is an abdominal tonsil. The destruction of cells and bacteria within the germ-centres of the tonsil, and the subsequent involution and disappearance of the germ-centres, points to the conclusion that one of their functions is the manufacture of immunizing bodies generally. As the germ-centres increase in number and activity in diseases which are certainly not bacterial in origin (hypo-thyroidism, hypo-pituitarism, hypo-adrenalism, malnutrition and digestive disease in children) as my observations conclusively prove, it is probable that they also provide the organism with substances to neutralize the toxins of defective metabolism.

(6) When the ductless glands, owing to the absence of essential nutriment, are unable to manufacture a sufficiency of hormones, the pharyngeal lymph units hypertrophy. The most careful examination of many thousands of sections of tonsillar tissue removed from such cases reveals not the slightest evidence of bacterial invasion. This statement is not based upon an isolated observation. In the course of the research my co-worker, W. E. Cooke, has cut some 20,000 sections from pharyngeal tonsils removed by myself. As a clinical cure is occasionally obtained in this particular type of hypertrophy by the administration of infinitesimal doses of iodine, it is possible that the organism attempts to force a simple lymph organ to do the work of complex endocrine glands which are functionally incompetent.

(7) Tonsillar hypertrophy constantly occurs at a time when the new-born child is not yet immunized; at a time, that is, when infection is most dangerous. Once immunization is effected both respiratory and alimentary tonsils normally tend to regress and disappear. As soon as the alimentary and respiratory tracts of the new-born infant are invaded by the innumerable micro-parasites which in the absence of immunity threaten existence, the lymphoid tissues, and particularly those of the respiratory tonsil, become enlarged, vascular and active.

Ætiology of adenoid hypertrophy

With regard to causes I shall confine myself to a brief summary of personal observations. Heredity is a predominant factor in about 50 per cent. of cases. Not only is it frequent to find the condition in several or all of the children of one family, but the facial appearance of one or both parents is often conclusive. The importance assigned to syphilis as a cause for adenoids by French writers is not confirmed. In one group of 600 adenoid children, there was one with specific nerve deafness, two with oxycephaly, twelve with true Hutchinson teeth, one with interstitial keratitis, but not a single case of septal osteitis, sabre-shin, or Hutchinson's syndrome of keratitis, notched incisors and nerve deafness.

There is no evidence that tuberculosis has any causal connection with adenoids, nor has there been any instance of an adenoid child with rickets. The skeletal deformities which afflict the adenoid child are chiefly confined to the respiratory framework; those of rickets are more generalized, involving the cranium proper and the bones of the pelvis and extremities. Breast-fed and bottle-fed children were about equal in number in more than one thousand cases, nor does sex appear to be a predominant influence, an equal number of boys and girls being affected.

Many children are born with adenoids. In such cases some or all of the following factors are usual:—(a) The environment of the mother during her pregnancy has been such that she has lacked a sufficiency of air and light; (b) her diet has been deficient in vitamins (particularly so-called fat-soluble A vitamin); (c) she has been subject to conditions which have produced extreme physical exhaustion, as, for example, having a bed-ridden relative to whom she attends in addition to working all day in shop or factory, doing her home work at night and taking in washing at the week-end. One or both parents and often grandparents are of the adenoid type.

Apart from heredity and such occasional determining causes as local or general infection, the common factor behind all cases of adenoid hypertrophy is malnutrition. The lungs of most of these children are fed upon the air-sewage of dark and badly-ventilated dwellings, and the diet is grossly deficient in essential food-factors. Not only the children, but the majority of the parents never eat butter, fresh eggs or unskimmed milk, and the cheapest fruit is an infrequent luxury. In many the diet is almost exclusively carbohydrate. Patent foods of the cheapest kind, fish and potato-chips fried in nauseating grease, together with butter substitutes and tinned carrion, form the diet out of which the physical bodies of many adenoid children and their ancestors have been built. Most of the diseases of humanity have been produced in animals by feeding them upon artificial foods.

Adenoid hypertrophy is a social disease, due to poverty, and the ignorance which accompanies poverty. Of the determining causes in any individual not actually born with the condition, the chief are the same as the predisposing causes, namely, improper food and foul air. In addition to these, or in their absence, the infectious diseases of childhood may act as determining causes in predisposed individuals. In a child in whom predisposition cannot be determined, any general or local infection which attacks the pharyngeal tonsil, as it might have attacked any other tissue of the body, is an accidental cause of the condition in another than the adenoid type.

Finally, with regard to the relative frequency of nasopharyngeal and faucial hypertrophy, in a series of 572 cases operated upon by the present writer, 15 had enlarged tonsils only, 282 adenoids only, and 275 both adenoids and enlarged tonsils. This preponderance of pathological conditions of the pharyngeal over those of the faucial tonsils, is an additional justification of the importance accorded to the former.

Treatment

During the past twenty years I have made many interesting observations on the purely medicinal treatment of adenoids. There is, to take one instance only, the effect of iodine. The minute quantity of iodine absolutely necessary for the harmonious working of the endocrine system is either absent from the diet of the adenoid child or cannot be assimilated in the form in which it is received. This deficiency may be partially rectified by the administration of infinitesimal doses of iodine, but only partially, for the condition depends upon more complex factors than the mere absence of this substance. Surgical removal is still the only efficient treatment, and will alone be described.

The indications for operation are too obvious to require elaboration. Whenever the pharyngeal tonsil becomes hypertrophied or infected it should be removed, irrespective of the patient's age. Failure to remove it results in the aural, respiratory and other disasters with which every practitioner of medicine is only too well acquainted. Apart from hæmophilia I know of no contra-indication.

In the present writer's opinion the La Force adenotome is the most efficient instrument that we possess for the removal of adenoid growths. I have used it in more than three thousand consecutive operations and have never had a hæmorrhage nor any other complication. A perusal of current laryngological literature proves that this happy immunity is far from being the lot of those who adhere to the curette. The La Force method, like any other surgical technique, has to be acquired. Failures to remove the growth by its aid are inconclusive, for they are merely evidence of an inaccurate technique, and in no way affect the results obtained by those who, after long experience, have abandoned all other instruments.

I have seen many failures of the popular curette to remove adenoids completely; the adenotome, on the other hand, never fails if correctly used. It removes the adenoid growth completely, usually in one piece,

and the removal is effected without injury to the pharyngeal mucous membrane or the Eustachian tubes. Pharyngeal trauma, with chronic sepsis and consequent ear disease, is a frequent result of curettage, and when the curette has been wielded by one of the many occasional operators who indulge in this operation upon the supposition that anyone can remove tonsils and adenoids the results are often more interesting than satisfactory. I instance only one woman recently seen at my out-patient clinic. Her soft palate had been torn through and her epiglottis damaged in an attempt to curette away her adenoids. This is an extreme case, but lesser degrees of injury are of frequent occurrence. Such disasters cannot be unusual; some such memory must have been in the mind of Dr. Dan Mackenzie when he wrote: 'In curetting excess of zeal is to be deprecated. There is no need to expose the pre-vertebral fascia, still less the bodies of the vertebræ'. He also writes: 'In the writer's opinion, the adenotome is unquestionably the best instrument', an opinion which is being shared by an increasing number of operators.

Failure to obtain perfect results with the La Force adenotome is due to one of two causes: (a) a faulty instrument; (b) an incorrect technique. Many of the adenotomes made in this country are wrongly constructed, particularly as to the angle of the adenoid box with the shaft of the instrument, which should be between 90° and 120°. If wider than 120° it is impossible to apply the instrument to the pharyngeal wall so that the whole of the growth is included in the box. Some adenotomes of foreign manufacture are made of inferior metal and must frequently be replaced; but they are usually correctly modelled and are often half the price of the incorrectly-modelled British instruments. Another disadvantage of some British adenotomes is the varied sizes of the blades; these should be interchangeable, but the blades made by one firm rarely fit the adenotomes made by another. To the laryngologist who removes adenoids as a daily routine this is a matter of importance. A correctly-modelled set of adenotomes, of British manufacture made to scale, with standardized blades, is an urgent need.

The faults of technique, which lead to failure when the instrument is of correct pattern, are two in number:

(1) The operator is so accustomed to the curette that he automatically makes a curetting movement with the adenotome as he pushes home the blade. This movement disengages the upper pole of the adenoid from the box. A portion of the growth thus escapes the cutting edge, and is left in the pharyngeal vault posterior to the upper edge of the vomer. This is the common fault of the inexperienced operator. It is not repeated when he realizes that the adenotome must be held absolutely motionless during the pushing home of the blade.

(2) The box of the adenotome must be pushed up into the vault of the pharynx. In order to effect this the shaft of the instrument must be maintained in pressure-contact with the incisors of the widely gagged lower jaw. If this contact of the shaft with the lower jaw is not rigidly maintained the instrument will fail to engage the upper portion of the growth.

Adenoidectomy by the La Force technique

(1) Under deep anaesthesia the gag is inserted to one side of the middle line of the jaw. If placed in the middle line, the thickness of the gag, one quarter of an inch, prevents the contact of the shaft of the adenotome with the lower jaw, and lowers the level of the box of the adenotome in the naso-pharynx by that amount.

(2) The operator palpates the naso-pharynx. He presses the folds of the adenoid growth together towards the middle, as one closes a half-opened book. He pushes any lower pharyngeal buds upwards, and any upper pharyngeal buds downwards, so as to crowd the contents of the naso-pharynx into a bunch which may be easily engaged in the box of the adenotome. At the same time he explores the lateral pharyngeal recesses (fossæ of Rosenmüller), breaking down any adhesions

about the torus of the Eustachian tube. These are sometimes so tough that the tearing of them is audible. They must never be curetted. If extensive, they may be rubbed away by a forefinger wrapped in gauze. Cutting or curetting may lead to incurable deafness from Eustachian obstruction.

(3) The adenotome is slipped under the soft palate, its box being pushed high up into the naso-pharyngeal vault. To effect this the shaft of the adenotome must be pressed down upon the middle line of the lower jaw.

(4) The blade is pushed home. This requires considerable force and when the adenoid growth is tough, as in adults, may require the strength of the surgeon's two hands.

It is absolutely necessary, during the pushing home of the blade, to press the box of the adenotome firmly and immovably upwards, against the vault of the naso-pharynx. If the adenotome is permitted to move or to slip, and particularly if any downward movement of curettage is made while the blade is pressed home, the result will be incomplete removal of the growth.

If removal is incomplete, one of three conditions will be found upon digital palpation: (a) the upper pole of the adenoid has escaped removal, (b) the lower pole of the adenoid has escaped removal, (c) both upper and lower poles of the adenoid have escaped removal.

These errors are remedied by a second application of the adenotome, so adjusted as to remove the fragments. It is never necessary to resort to the curette. Some authorities advise three applications of the adenotome, one to remove the central mass, and one at each side to remove the lateral masses. If the growth has been correctly adjusted by finger manipulation the whole of it will be included in the box of the instrument on its first application.

Attempts to remove lateral masses by deviation of the adenotome from the middle line may result in possible injury to the Eustachian tubes. Apart from lateral masses there are often adhesions in the fossa of Rosenmuller, but these should be broken down by the finger during the preliminary digital exploration already described.

It is important to use the largest instrument that can be pushed up into the naso-pharynx. One that will go in easily without any stretching of the soft palate is too small to engage the whole of the growth. The La Force adenotome, however large, cannot injure the Eustachian tubes, when applied in the manner described. It is a physical impossibility for the blade to cut through anything but the base of the growth. Further applications of the instrument to the side walls of the naso-pharynx are evidence only of the operator's failure to appreciate the object of the instrument, which is the complete removal of the pharyngeal tonsil, in one piece, by the one movement of pressing home the blade once only.

The Removal of Magnetic Intraocular Foreign Bodies

By F. H. VERHOEFF, M.D.

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It is a matter of common observation that flying missiles far less often strike the pupillary area than some other part of the cornea, but I have encountered few ophthalmologists who could explain this fact. The explanation, of course, is that the pupillary area is much smaller than the total remaining area of the cornea, so that the chance of its being struck is correspondingly less.

In the vast majority of cases, an intraocular foreign body is found to be magnetic even when the history seems to indicate otherwise. Usually the accident occurs when some object is being struck with a hammer, and, generally speaking, the smaller the fragment sent off, the greater its relative velocity and the greater its penetrating power. On the other hand, the smaller

the fragment, the greater the relative resistance it meets. Hence an intraocular foreign body is usually neither very large nor very minute. I have found that it is seldom more than 3 mm., or less than one-fourth mm., in its greatest dimension.

For obvious reasons, the size of the wound of entrance cannot always be relied upon as an indication of the size of an intraocular foreign body. Nor can the position of a corneal wound relative to a wound in the iris or lens be relied upon as an indication of the location of the foreign body, since, owing to some irregularity in its shape, the foreign body may swerve markedly while passing through the lens and vitreous. Many years ago an astute observer, whose name I cannot recall, made the observation that incarceration of the iris in a corneal wound was proof that there was no foreign body within the eye. I have met with few exceptions to this rule.

When there is a question of the presence of an intraocular foreign body within the eye, it is important to search for a hole in the iris. Sometimes it is impossible to recognise this by observing the surface of the iris by direct illumination, whereas it can be easily seen by throwing the light through the pupil and thus illuminating the iris from behind. If with the ophthalmoscope a non-perforating wound is seen in the fundus, it is almost certain that a foreign body is lying free in the vitreous chamber below. A small perforating wound of the sclera is sometimes invisible. In such cases an ophthalmoscopic examination often reveals more or less blood in the vitreous and thus indicates the advisability of an x-ray examination. I have seen many cases in which a wound of the cornea had been regarded as non-perforating and the presence of an intraocular foreign body overlooked. In some of these cases siderosis of the iris and lens capsule had developed while the patient was under observation. So far as I know, I have never made this mistake but possibly some of my colleagues could testify otherwise. It would seem to be unjustifiable to have an x-ray examination made in every case of apparent trivial injury to the eye, but if this were done fewer serious mistakes would be made. On the other hand, I have seen cases in which an intraocular foreign body had been carefully located by x-ray examination, when it could be plainly seen with the ophthalmoscope, and I have removed minute intraocular foreign bodies from eyes in cases in which x-ray examinations by experts had failed to reveal them. A localization of a foreign body close behind the globe should not be accepted without confirmation by a magnet test, and if possible, by ophthalmoscopic examination.

I have seen a few cases of xenogenous siderosis in which the patients were unaware that they had ever sustained injuries to their eyes. In my experience, after removal of a foreign body from an eye with siderosis, the vision is apt to continue to deteriorate to greater or less extent, owing no doubt, to iron remaining in the fluids of the eye.

Exact determination of the location of a foreign body in the posterior part of the eye is only exceptionally needed, since the same procedure for its removal is first tried no matter what its position may be. If the large magnet placed in front of the cornea fails to bring the foreign body forward, then a fairly exact knowledge of its size and position becomes important. Attempts to dislodge a foreign body by means of the magnet should not be abandoned until after they have been made on at least three successive days, for by repeated attempts the foreign body may be gradually loosened so that it may finally come away.

When an eye containing a foreign body is hopelessly infected no attempt, of course, should be made to remove the latter. A small hypopion, however, is not a contraindication to operation. In a number of cases after removal of a foreign body I have seen a hypopion one-half millimetre high rapidly disappear and normal vision return. Within recent years in all such cases of intraocular infection I have given daily subcutaneous injections of 20,000 units of diphtheria antitoxin. These

have been continued for a week unless in the meantime the infection has subsided or has become obviously hopeless.

For many years I have accepted the teaching of Haab that the safest way to remove a magnetic foreign body from within the eye is through the anterior chamber. Those who advocate removing it through a posterior scleral incision are, I believe, influenced chiefly by the facts that this method is simpler and does not require so powerful a magnet. The danger of subsequent separation of the retina is undoubtedly far greater after a scleral incision and for this reason the posterior route, in my opinion, should never be used unless it is found impossible to bring the foreign body from behind the lens, or there is a large open wound of the sclera.

I have made it a rule never to remove a foreign body through its corneal wound of entrance unless it is already engaged therein, because reopening a wound increases the scar formation and also increases the danger of infection. In a few cases I have made an exception to this rule when the wound was large and gaping, especially if it was near the limbus. In such cases the foreign body is, of course, large and the lens injured. A small magnet should at first be tried with the patient reclining, and the tip applied directly to the wound. By using a large magnet held at a distance, I have seen operators pull out the entire iris along with the foreign body. After the foreign body has been removed, as much lens matter as possible should be expressed through the wound. If the iris has now prolapsed an attempt should be made to replace it. If this fails, the prolapsed portion should be excised. A conjunctival flap over the wound is seldom indicated.

Before attempting to remove a foreign body from the vitreous chamber *via* the anterior chamber, it is important to dilate the pupil to the greatest possible extent. The patient is seated on a stool in such a position that the injured eye can be brought against the tip of the large magnet. He is then leaned backward until his eye is about two feet from it. The current is then turned on and the patient gradually brought forward until the magnet tip touches the centre of the cornea. If the foreign body has not appeared or the iris bulged forward, the current is repeatedly turned on and off. If this fails, the opposite pole of the magnet is tried in the same way and if this fails the magnet tip is applied at other parts of the cornea and at the limbus. This failing, an attempt should be made to bring the foreign body forward in relays. The eye is turned to one side if necessary, and the tip of the magnet applied to the sclera, first at a point close to the foreign body, and then over the pars plana of the ciliary body. If pain is now elicited, it is certain that the foreign body has come forward, and the tip of the magnet should again be placed opposite the centre of the cornea. As a result of one or another of these manoeuvres in many cases the foreign body will come around the lens and from behind the iris into the anterior chamber, but not infrequently it is held back by the iris. When this happens I employ a procedure that I described some years ago. I place the tip of the magnet at the limbus just in front of the level of the iris and just above an imaginary line which runs through the foreign body and is tangential to the pupillary margin. When the current is turned on, the foreign body will usually slide along the margin of the pupil into the anterior chamber. If it has become so firmly stuck in the iris that it will not come away, it may often be freed by applying the tip of the magnet at the limbus at a point near the foreign body; and then at the point just described. I have observed that in such cases many operators place the tip of the magnet diametrically opposite the foreign body. Owing to the resistance offered by the sphincter this procedure generally causes the foreign body to become still more firmly entangled in the iris and it may even cause iridodialysis.

After the foreign body is within the anterior chamber it of course sinks to the bottom of the latter. Until

recently I have always made the incision for its removal above, for the reasons that if post-operative prolapse of the iris should occur it would be preferable to have it do so above, and that it is less difficult to make a keratome incision here than below. I now believe, however, that these considerations are more than offset by the advantages of making the incision below, namely that the foreign body is below and that the patient naturally tends to look up during the operation. As a matter of fact, the danger of post-operative prolapse is negligible, owing to the small size of the incision necessary.

In making the incision, whether above or below, the point of the keratome should be entered as far back from the limbus as possible without danger to the lens or iris. If the incision is made too far forward, the shelf of corneosclera may prevent the foreign body from entering the wound. If the keratome is sharp, the incision can generally be made without obliterating the anterior chamber. If the latter is obliterated, it should be reformed by forcing salt solution into it with an irrigator. Otherwise, if the incision has been made above, the lens or cornea may be scratched by the foreign body. For a removal of the foreign body from the anterior chamber I have found a permanent magnet most convenient. It is important to draw the foreign body to the incision before inserting the tip of the magnet as otherwise the anterior chamber may be evacuated before the foreign body can reach the incision.

When the patient was a 'bad actor' and the lens clear I have employed either of two procedures. One consisted in having an assistant apply a small magnet to the metal handle of the keratome while I was making the incision. This kept the foreign body in the vicinity of the wound where it remained in case the anterior chamber was evacuated. The other procedure consisted of placing pillows under the shoulders of the patient so that his head was in such position that the plane of the iris was parallel with the floor. The foreign body was then drawn to the upper limbus where it remained when the incision was made. I now believe, however, that it is better to dispense with both of these procedures by making the incision below.

In exceptional cases a foreign body, after coming forward, becomes so firmly stuck in the iris that it is impossible to bring it into the anterior chamber. In some of these cases I have made the incision at the limbus near the foreign body, applied the magnet to the wound until a knuckle of iris prolapsed with the foreign body behind it. I then removed the magnet and snipped a small hole in the iris with scissors, and then again applied the magnet. In a few cases it was necessary to complete the removal of the foreign body by means of forceps in order to avoid too great traction on the iris. In others of these cases I have made a large incision at the limbus near the foreign body, pulled out the iris with iris forceps as if to do an iridectomy, and then removed the foreign body with the magnet. An objection to this method is that the iris is so greatly bruised that it becomes adherent to the lens. It is therefore important to replace it in normal position as otherwise the pupil may remain considerably distorted.

If the lens has been so severely injured that it would undoubtedly soon prevent any useful vision in the injured eye I remove it at the same time as I remove the foreign body. I make a large incision with the keratome, remove the foreign body with the magnet, then remove a large piece of the anterior capsule with the toothed capsule forceps, and then by expression and irrigation remove as much lens matter as possible. In this way the patient is spared a second serious operation and his total convalescent period is considerably shortened. On the other hand, if I think the lens may remain fairly clear for a considerable period of time, I delay its removal until it has become completely cataractous.

When a foreign body has lodged within the lens, both the foreign body and the lens should always be removed at the same operation. The operation, however, should be delayed until the resulting cataract prevents useful vision, unless siderosis of the lens capsule becomes evident before this. In a case in which a foreign body is embedded in the iris and has probably injured the lens, it would seem best to wait for a week or two before removing it, and to refrain from using a mydriatic. The delay may permit the wound in the lens capsule to become closed and thus prevent the formation of a progressive cataract.

A few cases present themselves in which it is not possible to use the anterior route. These include cases in which the foreign body is very large, or in which it is too small or too slightly magnetic to be attracted around the lens, and cases in which the foreign body cannot be dislodged by the magnet. When the foreign body is large, it generally has produced so much damage that the vision of the eye is destroyed sooner or later in any case. If the wound of entrance is through the sclera, and is still open, I remove the foreign body through it, if it is small and closed, I make an incision elsewhere as described below.

Many years ago I pointed out that theoretically the safest place to incise the globe posteriorly is through the pars plana of the ciliary body. This is anterior to the pars optica retinae, and even anterior to the vitreous, so that, for obvious reasons, there should be much less danger of post-operative retinal separation if a foreign body is removed through an incision here than if it is removed through an incision farther back. I have, however, seen separation of the retina follow removal of a foreign body through such an incision. In some cases this was evidently due to traction of the vitreous upon the retina at the site of the foreign body, and would, therefore, have occurred even if the anterior route had been used. In other cases it presumably was due to traction exerted upon the retina by vitreous which had been dragged into the operative wound.

Within the past few years, I have, I believe, made the operation still safer by incising the sclera gradually. Instead of plunging a cataract knife directly through the ocular wall into the vitreous as is usually done, I employ a large knife needle, the point of which has been filed off. A Post knife needle or a very large Knapp knife needle will serve. After dissecting up a conjunctival flap and inserting a suture ready to tie, with repeated sweeps of the cutting edge of the knife needle an incision is made in the sclera, parallel to the ora serrata at a distance of about 5 mm. from the limbus. Great care is taken not to incise the ciliary body. After the sclera is partly cut through, one edge of the incision is grasped with fixation forceps and the incision into the perichoroidal space completed by forcing the blunt point of the knife beneath the remaining scleral fibres and then cutting outward. The large hand magnet applied to the wound will now cause the ciliary body to bulge. If the foreign body is small and sharp it may at once come out through the ciliary body. If it does not, a small cut is made in the ciliary body and the magnet again tried. If the foreign body still fails to come out, the cut is enlarged to the extent necessary as found by repeated trials.

In rare cases the foreign body is so firmly embedded or encysted in the posterior ocular wall that it cannot be dislodged with the magnet. If it is sufficiently far forward, it may sometimes be removed by incising the sclera directly over it. The sclera should first be carefully incised, then a small incision made in the choroid, and the large hand magnet applied. If the foreign body presents itself but is held back by the scar tissue in which it is encysted, it may be grasped by forceps and freed by snips of scissors. If it does not present itself, a bent magnet tip should be inserted through the incision and carefully moved around in various directions. If a foreign body is encysted far back in the fundus, it is best not to attempt to remove it until

it begins to cause deterioration of the vision. In some cases it becomes so thoroughly encysted that good vision is maintained for many years. If it becomes advisable, an attempt to dislodge it may be made by passing a knife needle through the sclera just anterior to the ora serrata and picking at the foreign body while it is observed through an ophthalmoscope. This is, of course, a difficult procedure and must be carried out quickly, as the corneal epithelium rapidly becomes cloudy and obscures the view.

In a case in which the foreign body had penetrated the fundus about 6 mm. above the macula, and was partly within and partly outside the eye, I made an incision through the upper lid along the outer orbital margin, exposed the foreign body to view, and removed it with forceps. Excellent vision was maintained after the operation.

Thallium Acetate: Its Toxicity and Depilatory Action

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Clinical use and toxic effects.—In 1898 Combemale used 10 to 20 milligrammes for night sweats in patients with tuberculosis. He noticed that the loss of hair was rapid and complete. The next year Richet associated chronic poisoning with thallium and muscular atrophy.

Early clinical experiment.—A physician 37 years of age who took thallium for experimental purposes. He took one half to one gram every second day for three or four doses and then after two months he took several doses more. Nothing happened after the first experiment, but three or four days after the second, he noticed numbness in his fingers and toes and was taken to the hospital where his case was diagnosed as multiple neuritis.

Mechanism of action of thallium.—The remarkable action of thallium acetate in producing alopecia is so far as is known shared by no other substance. The exact mechanism of its depilatory action is not absolutely known, but certain established facts appear to show that this action is upon the sympathetic nervous supply of the follicles and not directly on the follicle or hair bulb itself. Endocrine glands are clearly concerned in the action of the drug. The post-mortem examination of the animals which had undergone prolonged thallium feeds revealed in all cases changes of an atrophic nature in the suprarenal glands, the thyroid and testes.

Thallium alopecia is directly due to the action of the salt on the hair-forming process. A series of histologic examinations of the scalp of patients treated with thallium show evidence of epithelial degeneration of the hair follicles and sclerosis of the connective tissue.

Animal experimentation.—Rat poison—zelio paste—which is 2.8 per cent. thallium, and zelio corn which is 2.1 per cent. thallium was mixed with the food; ill effects were noticed within from 16 hours to 4 weeks. Two weeks were needed for the loss of hair or alopecia. Examination of the rats and other animals showed degenerative changes in the central and peripheral nervous systems. There was a diffuse ganglionic disease. There was no damage done to any portion of the central nervous system. Schneider thinks that thallium acetate is very toxic. His opinion is that it is necessary strictly to limit its use. He reports that this thallium rat poison had been used by suicides and criminals with intent to kill.

Rat poison in the form of thallium sulphate was tested on sheep. The dose was 25 mg. per kilo of weight. The animals died on the 8th day. Doses of 10 mg. per kilo of weight were so small that the sheep survived but a noticeable slipping of the wool took place from the 13th day.

The symptomatology of thallium poisoning among the sheep included clamping of the teeth, loss of

appetite, general dejection, digestive disorders, muscular cramps in the hind legs, and coma. Death was due to respiratory failure.

Epilating action of thallium.—Drummond stressed the point of some biological and also practical interest in the fact that epilation following thallium leaves a narrow strip of hair across the forehead (the 'old Man's fringe') unaffected. It has been proved according to Drummond that this hair shows a greater resistance to external and internal irritation than other hair growths. The eyebrows likewise are unaffected. He asserts that thallium is highly toxic to adults and should not be given to them.

Feldon reviewed the statements and warnings regarding the intoxication from the use of thallium acetate in the treatment of ringworm of the scalp of children. He noted the peculiar fact that thallium cannot be used in the same dosage after the development of puberty without greater danger than in children. There is a marked increase in the toxicity which is probably due to the changed function of the endocrine-sympathetic system after maturity. He gives a report of two children, one a girl aged 15 who was completely infantile physically, size of child of 3 and only 35 lbs. in weight. Second child was a boy, a cretin, also infantile, age 19, but of the height of a child of 5 or 6 years. These two children showed only a slight epilatory effect which was insufficient to remove all of the infected hairs. This was undoubtedly due to the marked disproportion between age and body weight. The development of the endocrine organs possibly is parallel to the age and not to the body weight and if so the dosage made according to body weight does not correspond to the size of the endocrine organs.

Toxic action of thallium.—Several cases occurred of poisoning with suicidal intent from thallium in a rat poison sold freely in Vienna without a poison label. Characteristic symptoms in these cases consisted of pain in the joints, swelling of the feet and legs, colic, vomiting, sleeplessness, mental confusion, and a striking loss of hair from the head and body about three weeks after the administration of the poison. Too rapid administrations of thallium for therapeutic purposes has also been attended by toxic manifestations. The authors stated that a period of two to three months should elapse between the first and second administration of thallium. They write that it is possible to demonstrate thallium in the blood and urine within four weeks after the administration of a large dose. They mention that thallium is used in industry in the making of colours, window glass, and luminous paints, and that poisoning is possible from occupational contacts.

An attempted suicide spread half a tube of zelio paste on bread and swallowed it. The patient became ill two days later with pain and weakness in the lower extremities, albuminuria, loss of hair on the 11th day. She was ill for several months, suffering from peripheral neuritis, loss of appetite, pain in the chest, emaciation, depression, and amenorrhœa.

A number of cases of industrial thallium poisoning occurred in workers in a factory for the recovery of thallium. They had inhaled a powder (dust) of metallic thallium that is composed of thallium oxide and thallium sulphate. Besides alopecia, signs of poisoning manifested themselves in fatigue, anorexia, pains in the joints and lower extremities, albuminuria in nearly all cases, and a definite lymphocytosis of over 40 per cent. In one case there occurred after a month, heart burn and redness of the hair. Four months after beginning of regular work with thallium one patient showed a diminution of vision that progressed rapidly.

Cosmetic depilation with thallium.—Sabouraud as far back as 1897 suggested the use of thallium acetate as a depilatory. In 1912 he advocated the use of thallium acetate in 1 per cent. concentration once a day in a very small quantity and over a very small surface.

Sabouraud used thallium acetate in his service at the Hospital St. Louis to bring about a complete removal of the hair in children affected with tinea.

Sabouraud reported that thallium acetate by ingestion is capable of causing loss of hair in 15 days. It is not a harmless remedy and is to be used only under proper direction. He has shown that a paste of thallium acetate of 1 or 2 per cent. concentration applied every night to the lip and chin can within 6 or 8 months cause a reduction of the moustache or a commencing beard. The medicament should be used with care for one sees a number of cases of intoxication. It is essential to write the particulars of the dosage on the prescription. These are: Each evening treat only a small area of the total area of excess hair to be treated. The ointment must be applied by massage and the hands must be washed immediately thereafter with soap. The results will then be attended with little danger. All the accidents observed were among young girls who used the medicament in three times the dose advised. Grave toxic effects have been seen as temporary loss of all hair, temporary paralysis of the extremities, and nerve toxicity of several weeks' duration. Sabouraud was convinced that only those patients who did not follow his advice were the subjects of these accidents.

A 10 per cent. thallium cream has been used in hypertrichosis and sycosis, but an alopecia of the scalp frequently resulted with or without epilation of the area treated. A 10 per cent. cream was considered too toxic. Ionization has been utilized with a 2 per cent. solution of thallium acetate. It has been reported partially successful in hypertrichosis.

A commercial thallium depilatory.—A patient was reported to have used cream on the upper lip and under the chin. Two weeks after use of the cream she noticed pain in the chest, cramps, nausea, vomiting, and constipation; papuloid purpuric spots; hair of scalp was loose and easily pulled out; the eyebrows and eyelashes were not involved, but the scalp was completely bald except around the ears.

The formula for epilating cream as used by Sabouraud was—

Acetate of thallium	0.3
Zinc oxide	2.5
Vaseline	20.0
Lanoline			
Rose water	55 5.0

Further clinical reports.—A case was reported of thallium poisoning from prolonged use of depilatory cream. Patient had used the cream nightly for the preceding 5 months beginning its use 2 weeks before appearance of the first symptoms. A quantity sufficient only to cover the upper lip and chin had been used on each occasion. At each application the cream was well rubbed in. At the time of examination hair was distributed normally over the body with exception of the face where the growth was more profuse than is normal, and this hair was firmly imbedded.

Hair-growing properties of thallium.—The stimulating effect of small doses of thallium acetate on the rate of growth of hair in the rat has been noted. Single doses of 0.004 and 0.006 grams of thallium acetate per kilo body weight dissolved in distilled water injected intraperitoneally into white rats produced 18 per cent. increase in the rate of hair growth. Doses of 0.002 grams per kilo weight were too small to produce any effect on the rate of hair growth.

Absorption of thallium.—Dixon was definite that the symptoms of toxicity due to thallium depend on absorption. Thallium rubbed into the skin has no local action. Thallium is readily absorbed into the skin with alcohol or oil. It causes alopecia only after absorption. The effect is mainly on the autonomic motor system which is rendered more sensitive. However, this is more marked on the sympathetic portion, so that electric stimulation of the nerves produces an exaggerated response, even though the stimuli are below the normal response level.

Pathology of thallium toxicity.—1. The thallium preparations, by their influence on the vegetative nervous system, produce a series of changes on the latter, which in their turn act on the appendages of the skin, particularly on the hairs, causing a whole line of plethoric disturbances to the vessels of the hair bulbs, now in the shape of phenomena of an inflammatory character, with infiltration of round-cells; now again as foci of agglomerated cells, in the shape of furuncles.

2. Like all other salts of the heavy metals, such as mercury, bismuth and lead, thallium can produce a great many serious disturbances in the organism. These disturbances are as follows:

(a) In the skin, besides falling of the hair, folliculitis and a toxic eruption similar to the ones produced by mercury or bismuth, and of a hæmorrhagic character as petechiæ and ecchymoses.

(b) In the mucous membrane of the mouth, besides gingivitis, glossitis and stomatitis—even in its ulcerative form—the phenomena of an angina thallii. One also encounters cases of herpetic eruption, rhagades and sanguineous spots on the lips; and it should be noted that thallium can cause diarrhœas and sharp pains in the stomach.

(c) The mucous linings of the stomach and intestines show a picture of either stippled or completely fused hæmorrhages, besides one of either desquamative or ulcerative colitis.

(d) In the liver, we notice, besides hæmorrhages, thallium necroses and nephritis.

(e) In the liver and spleen, the phenomena are mostly of a vascular character. Besides rapid palpitations of the heart, we sometimes find paracardiac pains, which must probably be explained as due to influences from the vegetative nervous system.

(f) Acting on the vegetative nervous system, the thallium preparations can thus, through the latter, affect also the other branches of the nervous system, thereby producing those phenomena of quickly passing, epileptiform psychosis termed chorea. They can also act directly, and produce such phenomena as, for instance, thallium polyneuritis, disturbances of the blood vessels, including the periphæric blood vessels of the brain, and cerebral hæmorrhages.

(g) At the same time as the polyneuritic phenomena, one notices pains in the articulations, astragalgiæ, accompanied by swelling, tenderness and crackings.

(h) The disturbances thus described can be accompanied by pyrexia, and can cause the patient to become greatly emaciated and very weak, by changing the metabolism in the direction of a disaggregation of the blood-corpuscles already from the first dose of the thallium. They can also express themselves by interfering with the process of assimilation of the ingested food, a complication occurring especially in connection with serious disturbances in the intestine.

Retrobulbar neuritis.—Loss of sight as a result of thallium poisoning had been observed. Retrobulbar neuritis due to thallium poisoning from depilatory cream occurred in three patients. The cause of the toxic optic neuritides was not suspected at first. Each of the patients reported gave a history of the use of a proprietary depilatory cream.

The three patients were admitted to the neuro-surgical clinic as 'intracranial tumour suspects', and were found to have an advancing retrobulbar neuritis. Their failing vision was checked, and improved by discontinuing the employment of the thallium depilatory.

Therapeutic thallium for ringworm.—A number of children were examined at one time or another who had received the thallium acetate properly weighed for epilation of the scalp preliminary to antiseptic treatment for tinea capitis. One child was very ill with symptoms of intestinal upset, articular inflammation, marked pains in the chest, inability to hold food, loss of weight, and general debility. This patient required hospitalization.

The epilation of the scalp following thallium acetate was observed. The complete epilation of the pre-puberty group, and the partial epilation of the post-puberty group led me to frame the concept of nerve baldness. It appeared that thallium acetate probably acted through the sympathetic nervous system. The loss of hair was more nearly complete prior to puberty than after puberty was established. The control of the scalp hair of the entire scalp was under the sympathetic until puberty, and that the central nervous system then had a share. The recorded observation of Celsus made almost 2,000 years ago that persons with alopecia areata of the ophioid type (periphery of the scalp) offered a poor prognosis compared to those with loss of hair in the centre of the scalp was considered in this concept. Then, too, it is known that the borders of the scalp hair are more resistant to dye. Further, when a man loses his hair from the centre of the scalp in the pattern of the calvities Hippocratica, the hair at the periphery grows more rapidly so that the bald headed person must have less and less hair cut more and more often.

One of my assistants began the use of thallium acetate by ionization for the treatment of excess hair of the chin and moustache region. He did not finish the experiment because of the reports of toxic action by this method of administering the drug.

Animal experiments.—The reports that pilocarpine hydrochloride had the effect of growing hair when injected locally, given by mouth, or used as a scalp wash seemed to indicate that the action on the sympathetic nervous system of the pilocarpine and the thallium might be antagonistic. With this in view, a series of experiments were made:

Three guinea-pigs of about the same weight and age were selected. Pig one was given 8 milligrammes per kilo of weight of thallium acetate dissolved in water forcibly by mouth. Pig two received 8 milligrammes of thallium acetate and in addition one-twelfth of a grain of pilocarpine hydrochloride by mouth. Pig three received one-twelfth of a grain of pilocarpine hydrochloride alone. From theoretical considerations, pig one should have succumbed; pig two should have survived; and pig three should have been unaffected. Strange as it may seem, this was what actually occurred. Pig one died within eight hours after oral administration, and the other two pigs lived. The post-mortem examination was very brief—abdominal section. It was noted that the stomach was markedly enlarged with definite constrictions at the two orifices—the œsophageal and pyloric. These constrictions were so definite that removal of the stomach by section resulted in the removal of a stomach sac which did not leak any contents at either aperture. The stomach was opened, found to contain a large quantity of yellowish fluid. The mucosa was thinned.

The oral administration did not seem to be certain. The next three guinea-pigs were given the drugs in the same dosage by intraperitoneal injection. The pig which received thallium acetate alone died within the eight-hour period. The other pigs survived. The post-mortems were more complete—the brain case was opened, and the softening of the cerebral tissue noted; the chambers of the eye were engorged; the heart muscle was congested with pronounced hyperæmia; the lungs showed dilatation of the wall, the blood vessels, and extravasation of blood into the œdematous lung tissue; the intestinal walls showed areas of denuded mucosa, and extravasation of blood into the coats; the liver, spleen and kidney showed the same picture: œdema, widening of the blood vessels; and extravasation into the tissue of blood elements. The pathologic pictures were monotonous—and similar to those found by others.

The surprising repetition of the action of the pilocarpine hydrochloride in preventing the action of the thallium acetate immediately must be commented upon, but further experiments along the same lines have not given the same results. In the most recent experiments, the pigs receiving thallium acetate and pilocarpine hydrochloride died. The pathological findings were the same for both sets of pigs.

The main purpose of the experiments was to attempt to find if there was any antagonistic action between the two drugs. Our final conclusion is that none was really demonstrated by our work.

The pigs died too soon after the administration of the lethal dose of thallium acetate to expect any action on the hair. There was no effect noted. It is our opinion, that experimentation on the rate of growth of hair in the rodents is very difficult of control. The normal rate of regrowth after any procedure is very rapid. Local application of thallium paste to the skin of these animals must be guarded as it is impossible to prevent the animal from licking the paste and getting it into the system by this means.

SUMMARY

Thallium acetate and other salts of thallium have been recognized as toxic to man and animals from the time of the discovery of the element. Its use in night sweats disclosed the epilating action. Sabouraud attempted to make use of this action in the cosmetic removal of unwanted hair but found many untoward reactions and has guarded his prescriptions for this purpose. Many attempts to explain the epilating action of thallium have been made, but there is no agreement as to the mode of action. It seems accepted that the metal has an effect on the sympathetic nervous system, although a local action on the hair-forming process is claimed. The toxic action of thallium salts on animals has been used in poison potions for undesirable animals. Rat poison containing thallium has been used in criminal attempts to kill and by those desiring to commit suicide.

Within the past two decades, there has been a revival of the therapeutic action of epilation through thallium. Thousands of children have received the drug for the preliminary epilation of the scalp hairs to afford treatment of infestation with tinea organisms. Toxic effects due to the drug in proper dosage, and deaths from the inadvertent use of large doses because of poor mathematics or misunderstanding of orders have been reported. It is true that thallium is falling into disfavour, that is, in so far as its use as therapeutic epilatory is concerned for scalp hairs.

On the other hand, commercially minded concerns have taken advantage of the work of Sabouraud, and have placed before the public various thallium creams for the epilation of unwanted hair of the face and arms. Women are tremendously sensitive in our day and age to any hairiness. The sales of one American product which promised miracles at a high price were very large. Many women used this paste. Throughout the country, undiagnosed instances of thallium intoxication were treated for many conditions, but the rôle of thallium was soon uncovered. The physicians throughout the country have reported such unmasked thallium acetate poisoning.

My clinical experience and what few experiments I have done follow that of others in this field: thallium acetate as a depilatory does offer the opportunity of toxic action on persons using it whether for cosmetic effect (unwanted hair) or therapeutic action preliminary to antiseptic treatment of infested follicles with ring-worm or favus. Pilocarpine hydrochloride does not prevent the lethal action of a lethal dose of thallium acetate administered intraperitoneally into guinea-pigs.

It is our opinion, also, that many of the toxic results obtained from the external applications of thallium paste for the epilation of hairs of the upper lip or chin follow inadvertent oral administration. The application of the paste to the upper lip can easily lead to absorption by mouth. The very intimate contact of the upper lip and food or drink would permit of such absorption. The intermediate pillow case could also lead to such oral administration. The thallium acetate left on the massage fingers could easily be transferred to food eaten from the hand. Sabouraud recognizes this for he advises careful washing of the hands after the application is made.

The Aschheim-Zondek and other Laboratory Tests for Pregnancy

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THE researches of Aschheim and Zondek led them to conclude that the anterior lobe of the pituitary gland secretes two hormones which are intimately related to the functions of the ovaries. These two hormones, which they refer to collectively as prol-an, or individually as prol-an A and prol-an B, they regard as the stimuli of ovarian activity. Prol-an A induces maturation of the Graafian follicles; in the *liquor folliculi* of the mature follicles the presence of the hormone, variously called the female sex hormone, œstrin or theelin, has been demonstrated. Prol-an B is the term used to designate that factor in prol-an which effects luteinization of the follicles; and the *corpus luteum* produces the hormone progesterin, which causes the changes in the uterine mucosa before gestation occurs. Other investigators have failed to effect a separation of prol-an A and prol-an B, and incline to the belief that there is no real distinction between them. Collip has found in extracts from the placenta indications of three hormones which he believed to be distinct from those already mentioned. He has now found, however, that the one which he named emmenin is identical with œstrin. The question of the hormonal control of the reproductive cycle becomes obscure in the presence of all these factors. One clear fact that emerges is that conception is rapidly followed by a great increase in the quantities of prol-an in the blood and by its excretion in the urine. This is demonstrated by the injection of these fluids into immature female mice, a procedure which is followed by rapid maturation of the ovaries and precocious puberty. It is upon this fact that the Aschheim-Zondek pregnancy test is based. The technique of this test has previously been described in this journal and will be referred to only briefly here. Immature female mice receive six subcutaneous injections of the urine to be tested over a period of two days. One hundred hours after the first injection the animals are killed and their ovaries examined macroscopically for the presence of hæmorrhagic follicles and corpora lutea. The presence of these is diagnostic of pregnancy, whilst the finding of infantile ovaries rules out the possibility of pregnancy. The German authors claim an accuracy of nearly 99 per cent. in their results, which appear to be fully confirmed by workers in various parts of the world.

Many attempts have been made to reduce the time necessary for the completion of the test. Friedman observed that the intravenous injection of the urine of a pregnant woman into rabbits provoked ovulation. Since ovulation occurs in the rabbit only after coitus, Friedman's observation may be used as the basis of a test for pregnancy. Thus Reinhart and Scott developed a technique by which non-pregnant rabbits were isolated for a week and then injected with five to fifteen cubic centimetres of the urine of the patient in whom pregnancy was to be diagnosed. Laparotomy was performed on the animal after twenty-four hours. A positive indication of pregnancy was given by evidence of ovulation, as shown by the presence of hæmorrhagic follicles in the ovaries. If there was no evidence of ovulation and mature Graafian follicles were present, a further injection of urine was given and laparotomy was again performed twenty-four to thirty-six hours later. The non-appearance of hæmorrhagic follicles at this operation was considered a 'negative' reaction to the pregnancy test. From a discussion of the rabbit pregnancy test by White, Severance and others, it appeared that in order to attain the maximum accuracy with the test more than one intravenous injection was necessary, even in carefully selected animals. Also, the

animal must be examined at least forty-eight hours after the first injection to exclude false 'negative' reactions to the test although, of course, earlier indications of a positive reaction may be obtained by laparotomy.

Zondek has attempted to reduce the time taken by the Aschheim-Zondek test by alcohol fractionation of the urine, a procedure by which he concentrates the active principle six times. He examined the ovaries of the mice fifty-one to fifty-seven hours after the first injection. His conclusion is that a positive reaction is diagnostic of pregnancy, but that absence of reaction does not exclude pregnancy. He therefore always controls these results by carrying out the test with the ordinary technique. Ebersson and Silverberg also prepared by alcohol fractionation a concentrate of the active principle of the urine of pregnancy which effected maturation of the ovaries of immature rats. They performed post-mortem examinations of the animals forty-eight hours or longer after the first injection, but in an unspecified number of cases were compelled to resort to microscopic examination of the ovaries in order to reach a conclusion from the test.

Clinical application of the Aschheim-Zondek test.—The Aschheim-Zondek test has been used in this hospital as a diagnostic aid in a variety of conditions. In this connection 93 cases have been investigated. In addition, fifty-two tests were carried out as controls on the urine of patients known with certainty to be either pregnant or non-pregnant. Thus, in all, 145 tests were carried out, and in every case the result was correct. This remarkable accuracy leads one to place great confidence in the test.

Aschheim has pointed out that a positive reaction to the test occurs as long as the foetus lives and the chorion is in living contact with the mother's circulation. Within a few days of the death of the foetus the test fails to produce a reaction. In four cases in which a provisional diagnosis of dead foetus had been made, the two positive reactions were obtained from urine passed by the patient whilst the foetus was still alive or had just died. The specimens of urine failing to give reactions were passed by the patient a considerable time after the death of the foetus.

A quicker test for pregnancy.—The Aschheim-Zondek test has the disadvantage that the result is not available until one hundred hours after the commencement of the test. With the rabbit pregnancy test the result may be read forty-eight hours or less after the test is undertaken. Here the effect of the urine injections is merely to provoke ovulation by the already mature Graafian follicles, but in the mouse maturation of the follicles must first be effected before ovulation can occur. It was therefore believed that more rapid tests would be possible by means of mice if they were used at an age nearer to puberty than had been customary. With this end in view, sections of the ovaries of a large number of mice were examined. It was found that there was no evidence of luteinization of maturing follicles before the age of thirty-six days, and even at this age it was very rarely encountered. Macroscopically, all ovaries taken from mice up to this age appeared normally infantile. It seems permissible, then, to use animals of such an age that they shall be not older than, say, thirty-four days at the end of the test. With them, one would expect a more rapid response to the injection of the urine of pregnancy than with considerably younger animals.

Dickens has shown that prolan is precipitated from urine by concentrations of alcohol above 75 per cent. This observation has been used in concentrating the active principle in the urine during pregnancy in the following manner.

The urine, slightly acid to litmus, is mixed with three volumes of absolute alcohol and allowed to stand for thirty minutes. The mixture is centrifuged and the supernatant fluid is poured off. The precipitate is taken up in a small volume of water and the mixture is again centrifuged. The aqueous extract is found to be highly

active. Usually it is convenient to take fifty to sixty cubic centimetres of urine and 150 to 180 cubic centimetres of absolute alcohol. The precipitate may be spun down in a hundred cubic centimetre centrifuge tube in three spins, the supernatant fluid being discarded each time. After the final spin the supernatant fluid is decanted off and the tube drained for a few minutes or if the precipitate is bulky, the tube is placed in a water bath at 40°C. and exhausted for a few minutes in order to remove most of the alcohol. The precipitate is taken up with 1.5 cubic centimetres of distilled water and transferred to a 10 cubic centimetre centrifuge tube. The large centrifuge tube is washed out with three quantities of 0.7 cubic centimetre of distilled water and the washings are added to the 10 cubic centimetre centrifuge tube. After thorough mixing the insoluble portion is centrifuged out. The concentration effected by the procedure is about 15 to 1. In order that the final solution may contain as much prolan as possible, specimens of urine which are not too dilute are used. Usually the early morning specimen serves the purpose well.

Preliminary tests with the concentrates prepared in this manner showed that two injections of 0.3 to 0.4 cubic centimetre were sufficient to produce hæmorrhagic follicles in the ovaries of immature mice. Finally, the following technique was evolved and applied to a series of tests. The preparation of the concentrate from urine was commenced at 9 A.M. and was completed at 10-30 A.M. Four mice, twenty-eight to thirty days old, received two injections of 0.3 to 0.4 cubic centimetre at an interval of six hours. Fifty-five hours after the first injection, that is, at 5-30 P.M. on the third day, the ovaries of two of the mice were examined. If hæmorrhagic follicles were not seen, the remaining mice were examined early in the morning of the fourth day, that is, about seventy hours after the first injection. The finding of one hæmorrhagic follicle constitutes a positive reaction. In the absence of hæmorrhagic follicles the result of the test is 'negative'.

Tests were done in this manner with sixty-five specimens of the urine of pregnancy. All but six reacted positively at 55 hours. Of the six, five reacted positively at 68 to 70 hours. The one which failed to give a positive reaction either at 55 or 70 hours was a very dilute specimen of urine passed during the afternoon and was almost colourless. This single failure of the technique serves to stress the importance of using a well-coloured early-morning specimen of urine for the test. When this is done, the result of the test, if positive, is available in the great majority of cases in 55 hours, and, if no reaction occurs, in 70 hours. It is not suggested that this more rapid test should supplant the Aschheim-Zondek test. It is, however, a reliable test to use in those cases in which a quicker result is required.

The rabbit pregnancy test.—It has been suggested that it is a matter of greater difficulty to breed a sufficient number of mice for pregnancy tests than it is to use rabbits which are examined once or twice by laparotomy and used again when they have recovered from the operations. A more real advantage of the rabbit pregnancy test is that the result is available much earlier than in tests in which immature mice or rats are used.

In order to become acquainted with the rabbit pregnancy test, fourteen rabbits were used. They were segregated for some weeks to insure that they were non-pregnant, and then received two intravenous injections of ten cubic centimetres of urine at an interval of six hours. Forty-five hours after the first injection, the animals were killed and their ovaries were examined. The ten which had been injected with the urine of pregnancy all had hæmorrhagic follicles in the ovaries. The remaining four, which received injections of urine from non-pregnant women, had no hæmorrhagic follicles. Thus in this small series of fourteen tests, all the rabbits gave an accurate result. In those instances in which the test is urgent, the rabbits' ovaries could be examined

in twenty-four hours and a positive result would then end the test. As previously mentioned, however, the conclusion of White, Severance and others is that an animal showing no reaction at twenty-four hours must always be re-examined at forty-eight hours if 'false negative' reactions are to be excluded.

SUMMARY

(1) In 145 cases in which the Aschheim-Zondek test was used, the results were correct in every instance.

(2) A more rapid pregnancy test, based upon the Aschheim-Zondek technique, is proposed. The time taken by the test is 55 to 70 hours.

(3) Reference is made to a brief experience with the rabbit pregnancy test. Accurate results were obtained in all instances.

REFERENCE

White (M. R.), and Severance (A. O.) (1931). Comparison of Pregnancy Tests. *Journ. Amer. Med. Assoc.*, October 31, p. 1275.

Contraception : Its Justification and Practice

By DR. ELSA P. WOODROW

(Abstracted from the *South African Medical Journal*, October 22nd, 1932, Vol. VI, p. 653)

CONTRACEPTION, more popularly referred to as birth control, may be defined as the regulation of the birth rate by conscious control of human conception.

From earliest history the various countries of the world have been alive to the dangers of over-population. It was realized that, in a limited area, if the rate of increase was too rapid, the population would sooner or later outgrow the means of subsistence, and the growing pressure had to be relieved from time to time by the voluntary means of 'exposing' children, infanticide, abortion, and occasionally emigration. There were, in addition, frequent wars, epidemics and famines to act as involuntary checks on the increase.

On the other hand, certain conditions, such as improved cultivation, irrigation, and the growth of industry in towns, increased the material resources of the country and made a gradual increase of the population possible.

In the course of the nineteenth century, in countries such as Britain, a colossal change was brought about by the industrial revolution, whereby the enormous increase of material supplies resulting from the export of manufactured goods enabled a huge population to grow up. From 1800 to 1900 the population of England was more than trebled, and in Europe it increased from 187 millions to 400 millions. In the middle Victorian period the birth rate reached its highest peak of 36.3 per thousand.

A hundred years ago Malthus began to study and write upon the subject of population growth, and, in his 'Essay on Population', he advised his generation to avoid the terrible positive checks of famine, disease, infanticide and war by practising the prudential checks of postponing marriage and disciplining themselves in moral restraint after marriage—advice which has not found support from biologists, who for the most part, while acknowledging that some conscious control of conception is highly desirable and necessary, nevertheless consider these two methods as racially and individually bad.

Birth control has always met with considerable opposition from certain sections of the community. 'Race suicide' is a favourite catch-phrase on their lips, and 'Look at France' they usually add, and when we do look at France, as such opponents incidentally very seldom trouble to do, we find that in 1920, France, alarmed at the decrease of her population, accentuated by the ravages of war, passed an Act making the practice of contraception a criminal offence. The objects of this Act were not achieved, in that the number of live births did not increase, but the abortion rate

became appallingly high. Dr. Lacassagne, of Lyons, an eminent sociologist, estimated that the number of abortions in France rose to not fewer than 500,000 in a year, an appalling figure in comparison with the average annual total of 750,000 actual births!

Marcus Rubin, in 1900, in his work 'Population and Birth-rate, illustrated from Historical Statistics', shows that where the birth rate is very high, early mortality is also generally high, and therefore the survival rate is low. It is the survival rate which is the nationally important figure.

The mortality at all ages in Africa and Eastern Asia is far higher than among the less prolific races of Western Europe. It would seem, therefore, that birth control, as the most important alternative to a high death-rate, is an essential factor in human progress, and a necessary condition for the improvement of the racial type. The higher type will always be able to take care of itself against the lower types produced by unlimited procreation.

Birth control has, further, the national advantage of preventing the waste of maternal vitality and the financial outlay incidental to the production of weakly, diseased infants, which only too frequently become a burden to the State in later years, if indeed they survive at all.

Dr. Weinberg, of Munich, has shown by an analysis of 1,045 cases of very poor parents of the same class in Germany the value of spacing births. He found that where less than two years intervened between successive births from the same mother, the chances of life of the infant were almost halved, in comparison with those spaced at intervals of two years or more.

Margaret Sanger, the great pioneer of the birth control movement in the United States of America, shows clearly the difference obtaining in two countries which she visited. In one of these, Holland, birth control had been very generally practised for many years, and in the other, China, it had as yet made little headway.

In Holland the Neo-Malthusian League had, since 1881, established consultation centres all over the country. They were run by nurses and midwives specially trained for the work by Dr. Rutgers and Dr. Aleta Jacobs.

In 1915, when Mrs. Sanger visited the country, she found from the vital statistics that the tables of maternal mortality gave Holland the lowest figure, whereas the United States of America stood at the top of the list; also, the infant mortality rates of the Hague and Amsterdam were the lowest of all the cities of the world. There was no differential birth rate, as advice on contraception was available to all.

To turn now to the other side of the picture—China—I do not think I can do better than quote Mrs. Sanger's own words: 'In China the age-old injunction to increase and multiply had been carried to a literal conclusion. The ancient well-spring of art, philosophy, and the deepest wisdom of the world has been brought down to the lowest conceivable level by the brutal, bestial and squalid breeding of the worst elements of the yellow races. Pestilence, famine and war are the loathsome substitutes for contraception in checking the population growth.'

If the knowledge and practice of birth control could be extended throughout the world, it would not greatly alter the numerical proportion of the nationalities. A decline in the birth rate of each country would strengthen the nation by raising the health rate, substituting quality for quantity.

What we have to contend with chiefly at the present time is the differential birth rate obtaining in the majority of countries populated with Western European stocks. In a recent table of comparative fertility for England, referring only to women of child-bearing age, and taking the general population fertility at the arbitrary figure of 100, we get the following illuminating figures:—

Coal miners head the list with a fertility rate of 126.4. Agricultural labourers come next with 113.4, boiler-

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makers 110.1, farmers 100.5, Church of England clergymen 72, teachers 70.3, and lastly doctors 64.7.

There is only one remedy for this, and that is for the knowledge of birth control, and the facilities for its practice, to be available to all classes and sections of the community in equal measure.

It is a social issue of tremendous importance, and would prove one of the corner-stones in any scheme for the reduction of crime, pauperism, drunkenness and overcrowding. It would release vast amounts of time and money now spent in alleviating distress, ill-health and unemployment.

The movement for birth control has always had the opposition of the Churches to contend with, though their attitude has shown a somewhat less rigid disapproval in recent times.

It is a curious fact that their condemnation of effective methods of contraception is based on a biblical tale, 5,000 years old—the story of Onan, who was told to go and procreate children with his brother's widow, and who because he didn't wish to, had intercourse with her using the method of coitus interruptus to prevent the woman becoming pregnant. And this, we are told, 'was evil in the sight of the Lord, and he was slain'. The Churches have chosen to consider that the evil was the fact that he used a method of birth control, and not the fact that he was averse to following the tribal custom of marrying his deceased brother's widow.

In 1916, before the Birth Rate Commission in England, the Christian Churches, including that of Rome, made the statement that 'where all other deterrents fail, married couples may be allowed to limit intercourse to the intermenstrual period, sometimes called the *tempus agenosos*', or safe period. This, they declared, was 'natural', thus showing their profound ignorance of physiological laws, in that they allowed intercourse to occur when the woman was least inclined for it.

This method they also considered legitimate, because its success was uncertain. The line of reasoning is curious and somewhat obscure. They apparently consider that no sin is committed by using a method of birth control—a bad method too—so long as a loophole is left for the will of God to operate! This is birth control without its courage or science.

However, we have but to look back into history to encounter other similar theological opposition to the advances of science. An eminent divine, preaching against vaccination, declared: 'The law of God prohibits the practice, the law of man and the law of nature loudly exclaim against it'.

When Sir James Simpson fought for the use of chloroform in labour, the clergy were loud in denunciation of this 'unmitigated piece of iniquity'. However, it is good to realize that the Anglican Bishops at the Lambeth Conference of 1930 at last began to accept the modern trend of thought, which maintains that the birth of a child should be a rational process which has been planned and desired, and not merely the haphazard and unwanted result of sexual passion.

In their encyclical letter they declare that though 'there is a very strong tradition that the use of preventive methods is in all cases unlawful for a Christian, it must be admitted that it is not founded on any directions given in the New Testament'. Later on they say, 'We cannot condemn the use of scientific methods to prevent conception which are thoughtfully and conscientiously adopted.'

With regard to the Church's opposition to birth control, it is rather interesting to note that the clergy of the Church of England rival the doctors in their low birth rate, and the clergy of the Church of Rome are celibate.

Lastly, we come to the personal justification of birth control. No member of the medical profession can possibly be in ignorance of the results of unlimited procreation. We have all seen the poor wrecks of humanity that crawl up to the gynaecological departments

of our big hospitals, their lives one long agony of child-bearing, and each month a nightmare lest their periods should not appear. Ill and broken in spirit they come, these drudges of the world, ignored by governments and religions, reduced to a hopeless despair by the much-vaunted glories of motherhood.

It is no wonder that the women of the world have revolted against such abject slavery, that they are demanding to be something more than child-bearing machines, that they are demanding as their right a fuller and healthier life with opportunities for self-development and independence.

The appalling results of unrestricted procreation from the maternal point of view is not the only evil we have to contend with; it is not merely a question of birth control *versus* unlimited procreation, but birth control *versus* abortion.

The tale of self-induced abortions, with its trail of misery and ill-health, and its probable effect on maternal mortality and morbidity in later pregnancies, is a horrible reality.

In the *American Journal of Obstetrics and Gynecology* in the year 1922 it was stated that 'it has been estimated that in New York City alone there are 80,000 criminal abortions annually'.

Margaret Sanger, in the course of her nursing career, which took her into the poorest parts of New York, states she has seen on Saturday nights groups of anything from 50 to 100 women going into questionable offices well known to the community for cheap abortion.

But the world is awakening to the need for the dissemination of information on birth control. In England for ten years there have been clinics established on a voluntary basis in all the large towns, and in 1930 the Ministry of Health published its permissive memorandum allowing married women to be given information on birth control at the clinics, in cases where further pregnancy would be detrimental to health.

Municipal clinics are being established in certain towns for this work, and, in others, a grant is given to the existing voluntary clinics for the treatment of cases referred to them from the health departments.

Clinics are established in the United States, Germany, Holland and Russia.

In Japan, the health department of the city of Tokyo has decided to set up clinics in the municipal health advice stations. Japan is fortunate in that she has no religious conflict on the subject to contend with.

In Shanghai, two leading hospitals have volunteered quarters, staff, and equipment to educate physicians and nurses in contraceptive technique and in the direction of clinics.

In India, a Government birth control clinic has been established at Mysore, and the National Congress of Indian women, who are aiming towards the abolition of the traditional slavery of their sex, have realized that the knowledge of birth control is one of the most powerful weapons in their fight for freedom.

In South Africa, three clinics have been established in the current year. Early in February a clinic was opened in Johannesburg under the auspices of the Race Welfare Society, the mothers' clinic at Observatory was opened on February 15th, and in July a birth control clinic was opened in Pretoria.

Reviews

TREATMENT OF FRACTURES IN GENERAL PRACTICE.—By W. H. Ogilvie, M.D., M.Ch., F.R.C.S. In two volumes. The Pocket Monographs on Practical Medicine. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. 108 in volume I and from 109 to 180 in volume II. Price, 2s. 6d. each volume.

THESE little books attempt to give a practical outline of fracture treatment in the compass of 180 pages.

They are addressed to those in practice, and therefore the sections on anatomy, pathology and symptomatology have been curtailed to the minimum, in order to leave more space for those on treatment. Readers of 'Recent Advances in Surgery' will expect much from Mr. Ogilvie and they will not be disappointed. In the small space at his disposal he has managed to give an accurate summary of the most modern methods of fracture treatment, which puts to shame all the textbooks in general use. This branch of surgery has made great advances in recent years, owing to the more general adoption of methods of skeletal traction, made possible by the introduction of the Kirschner wire and the Steinmann pin. The teaching of Böhler has been adopted to a considerable extent, but the splints advocated are those familiar to British surgeons and the author is cautious in his recommendations for the use of unpadded plaster casts, though he advocates them for fractures of the leg and ankle he is not prepared to follow Böhler in other cases. For instance in difficult fractures of the radius and ulna he recommends operation in preference to traction combined with unpadded plaster casts, as safer, more scientific and allowing more perfect anatomical restoration. The teaching in this book is thoroughly sound and the amount of information compressed into such a small space is marvellous. The illustrations are rather rough drawings, but are very clear, it is a pity that figure 28 in volume II should be given as the treatment of fracture of the femur, whereas the treatment described in the text is correctly represented by figure 13, volume I; the former figure depicts a method now regarded as inferior. The book is one which may be strongly recommended to all practitioners.

W. L. H.

SURGERY.—By S. K. Sen, L.R.C.S., L.R.C.P. (Edn.), L.R.F.P.S. (Glas.). Vol. III. First Edition. Published by the Surgical Education Society, Ltd., Calcutta, 1931. Pp. iii plus 348. Illustrated. Price, Rs. 7-8 (per single volume).

THIS volume deals with surgery and pathology of growths. It consists of about 400 pages and is divided into six chapters. The description of the different varieties of tumour is very lucid and interesting. The subject-matter has been dealt with in a novel way, quite different from what we see in ordinary textbooks. The author's classification of growths into blastomatoids and blastoma is new, but it is for the pathologists to say whether this classification is sound or not. The summary at the end of each chapter and the marginal notes will help the readers to revise the subject. It is well illustrated and the author is congratulated on having a beautiful collection of photographs of his own cases. We miss very much the microscopical sections which should have been incorporated.

The get up of the book is nice, the type is good, but there are some spelling mistakes and repetitions of the same subject. We hope these will be rectified in the next edition.

The last chapter dealing with 'Diagnosis of Swellings' is really instructive.

S. N. M.

THE RATIONAL TREATMENT OF VARICOSE VEINS AND VARICOCELE.—By W. Turner Warwick, M.A., M.B. (Cantab.), F.R.C.S. (Eng.). Published by Messrs. Faber and Faber Ltd., London, 1931. Pp. 188. Illustrated. Price, 5s.

THIS is an excellent handbook consisting of 179 pages and divided into two parts each part having four chapters. The first part deals with the aetiology of varicose veins and the various theories in relation to this subject have been described briefly. The normal venous return, the connection between the superficial, perforating and the deep veins have been satisfactorily explained.

The second part deals with the different methods of treatment at present in use, both by operation and by injection. The author has fully described the actual procedure of the injection treatment, the various sclerosing solutions which are being used, their advantages and disadvantages, the emergencies that may occur and how to meet them. The appearance of this handbook in addition to similar handbooks on this subject shows the popularity of the injection treatment of varicose veins. The subject-matter is very thoughtfully conceived and the bibliographical references at the end of the book are very exhaustive and will be of great help to those who want to make a special study of the subject.

S. N. M.

ACUTE OTITIS MEDIA.—By W. M. Mollison, C.B.E., M.A., M.Ch., F.R.C.S. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. 71. Illustrated. Price, 2s. 6d.

THIS pocket monograph on acute otitis media and its complications, designed as a handy aid to the general practitioner, is sure to fill a want. Its seven chapters clearly written give not only an account of the anatomy of the middle ear, but also deal with the pathology of and types of acute middle ear disease with their treatment.

The last two chapters are useful ones in so far as the one places before the mind of the general practitioner in a concise way the complications that might arise in the course of an acute otitis media, and the other deals with acute mastoiditis and its complications.

The author is to be congratulated upon the complete way in which he has dealt with the subject in so short a space.

N. J. J.

THE DISCHARGING EAR.—By A. G. Wells, B.S., M.B., D.P.H., J.P., Barrister-at-Law. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. x plus 92. Price, 2s. 6d.

THE pocket monograph, *The Discharging Ear*, sets out very clearly the common causes of aural discharges and should be a great help to the general practitioner in the diagnosis of the various conditions which might lead to an aural discharge. The chapters are well written and an excellent account is given of the diseases of the external auditory meatus, the tympanic membrane, the middle ear and the mastoid process.

The paragraphs on treatment are particularly good and tell the general practitioner definitely what in the author's experience are the things to do.

The little book, I have no doubt, will be an acceptable addition to the literature already existing on the subject.

N. J. J.

ON THE CONSERVATION OF THE LYMPHOID TISSUE OF THE UPPER RESPIRATORY TRACT.—By T. B. Layton, D.S., M.S. (Lond.), F.R.C.S. (Eng.). Published by Ash and Co., Ltd., London, 1931. Pp. 46. Price, 1s.

MR. T. B. LAYTON in this monograph admirably argues the points in favour of conservative treatment. It must be admitted that operations for the removal of tonsils and adenoids are often hastily advised and alas more frequently done than is necessary. The author is to be congratulated upon the way in which he has proved the importance of the lymphoid tissue of the upper respiratory tract and the respect we should pay it. This little pamphlet should go far to lessen the wholesale practice of removing tonsils and adenoids which unfortunately exists to-day.

N. J. J.

LIPPINCOTT'S QUICK REFERENCE BOOK FOR MEDICINE AND SURGERY.—By G. E. Rehberger, A.B., M.D. Eighth Edition. Rev. ed. Philadelphia and London: J. B. Lippincott Company, 1932. Illustrated. Price, 65s. (Obtainable from Butterworth and Co. (India), Ltd., Calcutta.) Price, Rs. 48-12.

It is only a little less than two years ago since the seventh edition of this book was reviewed in these columns (vol. lxvi, p. 406). On this occasion we described it as the ideal book for the one-book medical practitioner. Very little change has been noted in the present edition. Additions and changes have been made in a few sections, including the sections on Addison's disease, angina pectoris, ascariis infection, brain abscess and injury, nervous dyspepsia, chronic colitis, vitamins, snake bite, syphilis, varicose veins, the diagnosis of pregnancy, erysipelas, oriental sore (but regrettably not kala-azar, though we drew attention to the defect in this section in our last review), radiography of the urinary tract, and rabies.

One cannot fail to be impressed by the general usefulness of the book. The very effective coloured illustrations of skin diseases and rashes, which the printed word is so powerless to describe, is perhaps the most outstanding feature of the book.

In recommending this book to the mofussil practitioner in India it is a pity that we are compelled to qualify our recommendation by saying that he will find it advisable to have another book on tropical diseases; with this qualification we recommend it whole-heartedly.

AN ATLAS OF SKIN DISEASES IN THE TROPICS.—By E. C. Smith, B.A., M.D. (Dublin), D.P.H., D.T.M. & H. (Eng.). London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. 60, with 253 figures in the text and 2 coloured plates. Price, 21s.

This atlas is composed of photographs and microphotographs of skin diseases that have been seen by the author in Nigeria. They have been well selected and considering the limited area from which they have been collected they represent a great variety.

All of the photographs are not of tropical diseases, such diseases as syphilis and tuberculosis being depicted; perhaps the best collection of photographs of a single type of disease are those devoted to ringworm. The author states in his preface that dark skins lend themselves well to photography for the purpose of displaying skin lesions and this is amply borne out by his results.

The letterpress is very brief, but with the accompanying photographs a good idea of most of the conditions is given. The book would have been easier to use if the numbers of the figures dealing with a particular disease had been placed at the beginning of the written description instead of in a list at the beginning of the book. Treatment is in many instances not mentioned at all and where it is included it is much too brief to be of use to any but the expert dermatologist.

Although the atlas is to a certain extent limited in its appeal to tropical practitioners in general, by the omission of diseases not seen in Nigeria, most of the diseases illustrated in the book are so widespread in the tropics that it will be a useful book to have at hand for ready reference wherever one may be practising.

In a book professing to describe the skin diseases of West Africa, it is surprising to find that there is no mention of crav crawl, not even as a synonym of scabies.

P. A. M.

SURGICAL PATHOLOGY OF THE FEMALE GENERATIVE ORGANS.—By A. E. Hertzler, M.D. Philadelphia and London: J. B. Lippincott Company, 1932. Pp. xxi plus 346, with 285 illustrations. Price, 21s. (Obtainable from Butterworth and Company (India), Ltd., Calcutta.) Price, Rs. 15-12.

This is the fourth of this series of monographs, which when completed will make a very fine and complete

encyclopædia of surgical pathology. The author claims that he has confined himself to his own experience; this has been a remarkably wide one. The book amounts to a very elaborate notebook of the life's experience of a surgeon, as far as this experience applies to the female generative organs. Every pathological condition is illustrated by a photograph or drawing of the part prior to operation, of the organ or tumour after removal, and usually of the histological section of the diseased area. A nice proportion has been maintained and the rarer conditions are dismissed with a few brief notes on the incidence, the symptomatology, the gross pathology, and the prognosis, whereas in the commoner conditions these matters are dealt with at greater length and other aspects, such as ætiology and histology, are included in the discussion.

The book is written by a surgeon, very definitely for surgeons. It is perhaps unnecessary in these days to impress upon the would-be surgeon the importance of a thorough knowledge of pathology. If any doubt remains on this point, one illustration in this book should serve to convince the doubter; this is an illustration of a carcinoma of the body of the cervical canal. Six months before removal, the cervix was found to be smooth and curettings from the body of the uterus showed no carcinoma; from the illustration it is easy to see why. By the time the uterus was removed it was too late to stop recurrences; an earlier removal would probably have effected this.

The book will form a valuable addition to the library of the general surgeon or the gynaecologist.

DIAGNOSIS AND TREATMENT OF DISEASES OF THE THYROID GLAND.—By George Crile and Associates. Edited by A. T. Rowland. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 508, with 164 illustrations. Price, 32s. 6d.

THE compilers of this new book on the thyroid gland do not claim that it is a formal treatise on the subject, but an account of the experience of the Cleveland Clinic with the diseases of this gland. Nevertheless, as the members of this clinic are open-minded workers who have not hesitated to use the experience of their confrères in other parts of the world to add to their own, and as every aspect of the subject is dealt with by one or other of the contributors, the book does in fact amount to a treatise on the subject.

The chapter on iodine and the thyroid gland forms a very satisfactory introduction. The figures that appear in this chapter give one a clear idea of the histology of the various forms of thyroid disease, and there is an excellent summary of our present knowledge on the association between iodine and goitre.

There are 39 chapters, so that it is quite out of the question even to give the chapter headings here. The chapters on operative technique are very well illustrated and each step in the operative procedure is given in detail. American workers have a way of ignoring work done in India; it is, therefore, gratifying to see that McCarrison's work has been referred to freely. The authors have produced a valuable reference book on thyroid disease.

THE BIOCHEMISTRY OF MEDICINE.—By A. T. Cameron, M.A., D.Sc., F.I.C., F.R.C.S.E., and C. R. Gilmour, M.D., C.M., F.R.C.P. (C.). London: J. & A. Churchill, 1933. Pp. x plus 506, with 31 illustrations. Price, 21s.

THIS book is the result of a happy co-operation between two authors, one a professor of biochemistry and the other a professor of medicine and clinical medicine. It is designed both for the student of medicine receiving clinical instruction in the later years of his course, and for the physician who received no special instruction in the medical applications of biochemistry. The modern system of specialisation divides the different branches of study into water-tight compartments and it is often difficult for the student to receive sufficient direction to enable him to co-ordinate pure biochemistry with its different applications to medicine.

A book of this kind is designed to help such a co-ordination. Again, modern medical literature contains a large volume of papers dealing with the biochemical studies of diseased conditions and it is becoming increasingly difficult for one to be abreast of the advances of medical science. This book is, therefore, the more welcome to one who desires to keep himself informed about the outstanding biochemical work which has contributed definite facts of value to medicine. The authors have introduced a small amount of biochemistry of the normal man in order to make the biochemistry of the pathological states more intelligible to the reader. After introducing the normal carbohydrate metabolism, the normal metabolism of fats and other lipoids, the different types of non-diabetic glycosurias, the sugar-tolerance curves and their significance have been discussed. The subject of diabetes mellitus has been treated in fair detail. The abnormal metabolism of fat (other than in diabetes), the normal and abnormal metabolism of water (including a discussion on oedema, albuminuria, nephritis, uræmia, etc.), the metabolism of inorganic compounds and ions, respiration and respiratory disorders, the functions of the organic compounds of blood and diseases associated with them (like anaemia, jaundice, etc.), the endocrine secretions and their functions, the vitamins and vitamin-deficiency diseases, and finally the gastric functional tests and liver functional tests form very interesting reading. A short summary at the end of each chapter helps the reader to recapitulate the important facts discussed in each and there is a short bibliography at the end of each chapter dealing with the recent literature on the subject. Rather more space than necessary has been devoted to the rarer anomalies of disease at the expense of the commoner ones, but the authors point out that many of these rarer conditions and diseases are found to be less rare now that adequate biochemical tests for their detection are being employed, and further, little or nothing of value can be said, biochemically, concerning many of the commoner diseases, like tuberculosis, cold and cancer. Although there are some good books on allied lines the present volume is a welcome addition to medical literature. It will not only help a more intelligent study of medicine in the light of the most recent advances of biochemistry, but will stimulate newer ideas of research.

S. G.

PREVENTIVE MEDICINE.—By M. F. Boyd, M.D., M.S., C.P.H. Fourth Edition. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 532, with 149 illustrations. Price, 22s.

THIS is a book intended primarily for medical practitioners in the United States of America. It will be remembered that the General Medical Council of Great Britain in their review of the medical curriculum in 1920 stated in regard to the teaching of hygiene and preventive medicine, that these were principles and concepts and not merely 'subjects', and that the teaching of preventive medicine should permeate the whole of medical education. The general practitioner must develop the preventive outlook, and preach and practise it in his profession. In the United Kingdom, the practitioner has already been brought into the scope of preventive medicine by his obligatory participation in much of the legislation of state medicine. In this connection one can instance the National Insurance Act, the Notification of Births Act, the Tuberculosis Regulations, the Factories' Acts, the Venereal Diseases Act and Regulations and many others. In the United States of America, legislation in state medicine has not yet included the general medical profession so comprehensively. The application of preventive medicine in every-day life has rather come from the large insurance agencies like the Metropolitan Insurance Company, which now has a large number of medical practitioners on its staff carrying out preventive medical examinations and inculcating principles of health and preventive medicine amongst their clients. This is all

to the good, and one frequently sees the opinion expressed in the United States, that the physicians there are neglecting their opportunities in preventive medicine, and that if this neglect continues the opportunities will lessen, and the field will be taken away altogether from physicians by a changing public sentiment.

The book under review is intended to supply the student of medicine and the general practitioner of medicine with the minimum knowledge of the subject which they should be expected to possess. In this Dr. Boyd has we think succeeded admirably. The salient and important facts of personal and communal hygiene are presented interestingly and shortly, and the book is saved from being a mere summary by the excellent style of the author, and by the authoritative view he is entitled to express not only as a malarialogist, but as a member of the Public States Board of Health. Students of public health in any country will find the book very useful as an up-to-date record of essentials. There are many excellent illustrations which enhance its value. The printing, paper and binding are excellent.

A. D. S.

MICROSCOPIC SLIDE PRECIPITATION TESTS FOR THE DIAGNOSIS AND EXCLUSION OF SYPHILIS.

—By B. S. Kline, A.B., M.D. London: Baillière, Tindall and Cox, 1932. Pp. 99 plus xviii, with 28 figures in the text. Price, 13s. 6d.

IN this small work the author describes his precipitation test for syphilis, the first paper on which was published in 1926. His test is a modification of Kahn's test, though the antigen is somewhat differently prepared. The Kline test is performed microscopically. A critical discussion of the contents of this work would raise the large question of the relative advantages of the Wassermann and flocculation tests for syphilis, which would be out of place in a brief review. The main question in the diagnostic use of the flocculation tests is what clinical value to attach to comparatively small differences in the degree of flocculation. In this, experienced interpretation no doubt plays a great part. Some of the author's technique is decidedly ingenious and he has carried out a useful piece of research in investigating the optimal conditions for flocculation tests. We are not convinced that there is any great advantage in performing flocculation tests for syphilis microscopically, except possibly in infants where there is difficulty in obtaining sufficient serum for tube tests by drawing blood from a vein. Nor do we see much advantage in a very rapid test. 'Immediate' diagnosis of syphilis is only exceptionally of value, e.g., in the testing of a blood donor or in the examination of urgent conditions such as cerebral thrombosis. Apparently the Kline test is as good as any other flocculation test. The value of the tables on pp. 70 and 71 showing comparative results with the Wassermann and Kahn tests is greatly reduced by the fact that more than seventy-five per cent. of the sera examined were from non-syphilitic conditions. It is evident that the larger the proportion of non-syphilitic sera in any series, the greater the percentage of concordance between the results of the tests examined is likely to be. The illustrations are good, but we frankly do not care for the type of diagram favoured by the author. Some of the diagrams, e.g., that on p. 2, seem more suitable for elementary lectures than for inclusion in a work which is intended for specialists. The book is well written, the practical directions are clear and there is much which will repay careful study. A word of praise is due to the publishers for the convenient format and good appearance of the work.

R. B. L.

CLASSIC DESCRIPTIONS OF DISEASE.—By R. H. Major, M.D. London: Baillière, Tindall and Cox, 1932. Pp. xxvii plus 630, with 127 illustrations. Price, 30s.

THE author claims that he was stimulated to write this book by reading *Selected Readings in Pathology*

and *Selected Readings in the History of Physiology*. It was certainly his experience with these two books which led the reviewer to undertake his present task.

This book is larger and its scope is wider than that of the other two books mentioned above. The readings are not arranged historically, but in sections each dealing with a different group of diseases, e.g., Infectious Diseases, Diseases of Metabolism, etc. Needless to say the grouping is done according to our present-day knowledge not according to the state of knowledge at the time many of the writings were dated, in most instances, but there are exceptions; for instance under the heading 'Respiratory Diseases' is a description of Cheyne-Stokes breathing, by Hippocrates, in what appears to be a case of blackwater fever. Except for a few facsimile reproductions the descriptions which were not originally in English are translated.

For no very obvious reason Paracelsus has always made a particular appeal to the imagination of the reviewer; he has always felt that a man who was born with the names Theophrastus Bombast von Hohenheim, who added the names Philippus Aureolus, and who then adopted the pseudonym Paracelsus was no ordinary individual. This sixteenth century physician has received a considerable amount of attention in this book and his writings on cretinism and endemic goitre have been reproduced extensively, to the great satisfaction of the reviewer.

There are a few criticisms to be made. The author has not adhered to the scope defined in the title. There seems to be very little justification for bringing Banting into a book entitled 'Classical Descriptions of Disease'; however epoch-making was Banting's work, none of it could be classified under this heading. Still, the fault, if it exists, lies in the title and not in the book. This constitutes a very important contribution to the history of medicine, and we must congratulate the publishers on adding this to their already imposing list of books chronically the milestones in the advance of medical science. The format of the book is particularly pleasing; the sombreness of the ordinary medical book has been avoided without an undue lapse into frivolity.

L. E. N.

A SHORTER HISTORY OF SURGERY.—By Sir D'Arcy Power, K.B.E., F.R.C.S. (Eng.). London: John Bale, Sons and Danielsson, Ltd., 1933. Pp. 91. Price, 3s. 6d.

THIS is a very small book—of about 25,000 words. It amounts to little more than an essay on the subject. It is however a very well-balanced essay and it should certainly achieve the object for which it was written, namely, to give the reader a taste for more—it is in fact a sort of *hors d'œuvre*.

The history of surgery is essentially the history of medicine, up to the beginning of the 19th century; from that date onwards specialization began to creep in. There are some very unpleasant patches in this history up to the time of Lister. His introduction of antiseptic methods coincided more or less with the introduction of anaesthesia, and from this time onwards the march of surgery has been triumphal.

The book contains little new matter, but the old matter it presents in a concise and pleasant manner. We can strongly recommend it to our readers.

L. E. N.

1. MODERN BIRTH CONTROL METHODS OR HOW TO AVOID PREGNANCY.—By G. R. Scott, F.P.H.S. (Eng.), F.Z.S. London: John Bale, Sons and Danielsson, Ltd., 1933. Pp. x plus 209. Price, 7s. 6d.

2. EUGENICS AND BIRTH CONTROL.—By Mercia Heynes-Wood (Mrs. Cedric Dover). Second Edition. Lahore: The Times Publishing Co., 1932. Pp. 119. Price, Rs. 3.

THE literature on birth control is enormous and is added to almost daily. The sale for books on this

subject must be equally large or the law of supply and demand would operate and stop the flow.

Mr. Scott's book is like many others, but on the whole it is a very satisfactory book. It lives up to its title, and its sub-title, 'How to avoid pregnancy'. Little time is spent in discussing the ethics of birth control; the author goes straight to the point and describes various methods, giving their *pros* and *cons*. He ends with a table covering some 12 pages, in which the indications, the contra-indications, the reliability, etc., of the different methods are given. One interesting feature is that the writer does not condemn, except on the grounds of unreliability, *coitus interruptus*, as most writers do; his reasons seem sound enough.

The fact that there was a foreword by Sir W. Arbuthnot Lane did not increase the reviewer's confidence when he undertook his present task, nor in his opinion has the foreword added to the value of the book; many people will disagree with this prolific contributor to the lay press when he states that a man's or a woman's general usefulness in the world is in proportion to his or her sexual development. Otherwise, the book is a practical one and can be recommended.

Mrs. Dover's book is written for the Indian public, both domiciled and indigenous. The subject is discussed mainly from the point of view of India, and the wider aspects of the problem of population control are dealt with. A number of pages are devoted to the technique of birth control, but there do not seem to be any methods particularly suitable for the Indian ryot, who, if it is population control rather than birth control that is the desired goal, is the person to whom the methods must be applicable. The author has taken a sane view of the subject and the book should prove useful.

SIMPLIFIED DIABETIC MANAGEMENT.—By J. T. Beardwood Jr., A.B., M.D., F.A.C.P., and Herbert T. Kelly, M.D., A.A.C.P. Philadelphia and London: J. B. Lippincott Company, 1932. Pp. 191. Illustrated. (Obtainable from Butterworth and Co. (India), Ltd., Calcutta.) Price, Rs. 4-8.

SIR Dr. Lawrence described his 'line ration' scheme in the dietetic treatment of diabetes, several other simplified processes for the calculation of diabetic diets by the rule-of-thumb method have been advocated.

The special feature of this little book lies in what the authors describe as the 'unit method' of measurement of diabetic diet. According to the authors, this system of measurement, when used in conjunction with the diet-prescription charts given in the book simplifies calculation of the diet from the doctor's point-of-view and makes the actual measurement of the diet easier for the patient.

The method is spread over three groups which are called A, B, and C. In group A, each unit consists of 5 grammes of carbohydrate and 1 of protein, having a caloric value of 24. In group B, each unit consists of 5 grammes of protein and 10 of fat, having a caloric value of 110. In group C, a unit consists of one unit of group A and one of group B, or 5 grammes of carbohydrate, 6 of protein and 10 of fat, with a caloric value of 134.

The book is divided into three chapters. In the first chapter the author has dealt with general considerations, so as to enable the patient to co-operate intelligently with his doctor. Chapter II deals with the symptoms, the diagnosis and the treatment of diabetes including complications that arise. In the last chapter, the author has mainly dealt with the 'unit' method of calculating diabetic diet and has given illustrated charts together with specimen diet charts and diabetic recipes.

The book should prove to be of interest to both diabetic patients and doctors.

J. P. B.

MATERIA MEDICA FOR NURSES.—By A. Muir Crawford, M.D., F.R.F.P.S.G. Second Edition. London: H. K. Lewis and Co., Ltd., 1933. Pp. viii plus 89. Price, 3s. 6d.

THE second edition of this book will be welcome to members of the nursing profession. It is a small book covering about 100 pages, written in an easy and readable style. The author has used considerable judgement in selecting only drugs in common daily use with their important preparations, doses, actions, and therapeutic uses. *Materia medica* is a vast subject, growing every day in volume, and it is no easy matter to pick out only the essential requirements for the nurses without going too far into the unnecessary details. The chapter on classification of drugs according to the part of the body upon which they act is worth special mention. The table of important doses at the end will be useful for ready reference. Several drugs included in the new edition of the British Pharmacopœia have found a place in the book. It can be recommended as a good textbook for nurses.

R. N. C.

THE BREAST-FED BABY IN GENERAL PRACTICE.—By L. G. Housden, M.B., B.S. (Lond.). London: H. K. Lewis and Co., Ltd., 1932. Pp. viii plus 118. Price, 4s. 6d.

STATISTICS of the admission of infants to the medical wards of the Great Ormond St. Children's Hospital are convincing evidence of the value of breast feeding. Of the babies admitted 88.5 per cent. were bottle fed and only 11.43 per cent. breast fed. Figures indicating such a high degree of morbidity amongst artificially-fed babies should cause the family doctor to pause and consider before countenancing or actually encouraging the mother to wean her baby. The immediate results of artificial feeding are, perhaps unfortunately, often

good, and it is certainly easiest and most time-saving for the busy practitioner to recommend a bottle, but there are many cogent reasons against it and Dr. Housden should have little difficulty in accomplishing the object of his book, namely, to pass on his conviction alike of the necessity and the possibility of promoting breast feeding even in a busy practice.

He deals practically with the causes of failure, the difficulties encountered in general practice, the management and technique of successful feeding, and the anxieties aroused by breast-fed babies. He has some interesting observations to make on the best time for the first feed, and advocates as a result of experiment that it should not be given earlier than 24 hours after birth. The chapter on methods of increasing the quantity of milk secreted contains a fairly complete account of a new method—the hypodermic injection of 1 cubic centimetre of human milk—which Dr. Housden has found to be of definite value in selected cases.

Vitamine A is said to be found in oils without any qualifying adjective, and cows' milk is said to be four times as rich in iron as human milk, whereas it contains half to one-third as much.

The essay, 'Studies in breast feeding', incorporated in *The Breast-fed Baby in General Practice*, was awarded the Sir Charles Hastings' clinical prize by the British Medical Association in 1932. That is sufficient evidence of its value and usefulness, and the book needs no other recommendation.

J. M. O.

PATHY BIDHI, OR DIET. (Written in Bengali).—By B. B. Pal, L.M.S. Published by Dr. B. B. Pal, L.M.S., Armanitola, Dacca, 1932. Price, Re. 1-8.

THIS little volume sets forth clearly and concisely useful hints regarding the diet in relation to different common ailments of the body in Bengal.

S. P. B.

Annual Reports

THE ROCKEFELLER FOUNDATION: ANNUAL REPORT FOR THE YEAR 1931. NEW YORK.

FOLLOWING its extensive early hookworm programme and its emergency tuberculosis work in France, the Foundation in 1920, or a little over ten years ago, began to participate in the public health work that was being re-established on a peace-time basis in many parts of the world. Two general purposes have underlain the many forms of public health work in which it has participated: the first of these is the acquirement of new knowledge in hygiene and public health by field and laboratory research; the second, extension of such knowledge through application of what is already known. In a number of countries there has been brought about, partly through the Foundation efforts, a considerable investment in men, ideas, buildings, and equipment, now representing a constructive force in the public health work of the world.

During 1931 the Foundation assisted the governments of forty-seven countries throughout the world and the health administrations of thirty-seven states in the United States in carrying on public health work. Aid was given to local as well as central health services. Contributions were continued to the Health Organization of the League of Nations, which is active in the international interchange of public health personnel and in maintaining a world-wide system of public health statistics and an equally wide service of epidemiological intelligence. In addition, the Foundation engaged in certain activities in connection with tuberculosis, respiratory diseases, undulant fever, and anæmia, and in epidemiological studies and studies of sanitation and public health service.

Yellow fever

When for the first time in history a laboratory animal, the rhesus monkey, became available for yellow fever studies, the disease itself began to yield some of its secrets. It was revealed as a virus disease which could henceforth be properly classified with other virus diseases, of which there are a great many in the plant, animal, and human worlds, two of the most common being smallpox and the ordinary cold. An even more important revelation was that of its wide-spread existence in mild form, impossible of detection by ordinary medical methods. It became clear that the conspicuously successful campaigns referred to above had dealt with yellow fever in its virulent form, the form it takes when it leaves its native lair and rages among new, non-immune populations; they had but pushed the disease back into the remoter parts of the world from whence it had come. The insidious nature of yellow fever masquerading as a mild affection among distant native populations stood out as a new factor. With the further aid of the monkey there was made the beginning of an attempt to chart the regions in which this mild form of yellow fever lurks and from which it may at any time break forth to work its well-known havoc among the other populations of the world. There is, moreover, full realization that this danger has been enormously increased by the greater rapidity of land, sea, and air travel and the rising susceptibility of populations in regions which have been freed of yellow fever.

The hazards attending any attempt to beard yellow fever in its own den, both in Africa and in certain regions of South America, have been amply demonstrated

by the numerous deaths occurring among scientists engaged in this task. Some method by which it might be possible to interrupt this series of deaths among laboratory workers has been urgently needed, and there is every indication that a good step forward in this direction has been taken by the development of a new vaccine against yellow fever, based directly on the use of white mice. It is a pleasure to note that this year The Rockefeller Foundation does not have to report any deaths from yellow fever among its personnel. No fatalities from the disease occurred among the staff during 1931.

The first vaccination of a human being against yellow fever by the new method occurred on 13th May, 1931. Thus was brought to swift preliminary fruition the yellow fever laboratory work with the mouse, the second animal to help man in his conquest of yellow fever.

Yellow fever in the mouse bears little resemblance to yellow fever in man. In the mouse it takes the form of an encephalitis. In this animal the virus is neurotropic, instead of viscerotropic as in man.

The next step was to stabilize the virus, so that scientists would have available a substance which was uniform in its reactions and capable of producing the desired effects with certainty. After many passages through mice, the virus becomes highly virulent for these animals, and the incubation period becomes short and constant. At the same time the virus loses its power to kill rhesus monkeys, although it does continue to produce fever in these animals; in other words it assumes the character of what is known as a fixed virus.

With a virus having stable and dependable qualities it was possible to develop further a protective procedure involving inoculation with yellow fever virus and the simultaneous administration of yellow fever immune serum. It was shown that these combined infections developed active immunity in monkeys. Presumably they would do the same to human beings.

This has been verified. Between 13th May and 29th June, 1931, ten persons were vaccinated. Before vaccination the sera of these persons were without protective power, i.e., they did not protect from death animals inoculated with yellow fever virus. After vaccination the sera from these persons, in every case, had protective power against yellow fever virus both in monkeys and in mice. Persons who have been vaccinated are in the same class as persons who have had yellow fever. Since it is well-known that anyone who has survived an attack of yellow fever is immune to the disease for the rest of his life, vaccinated persons are presumably similarly protected, but time will be required to determine with exactness the duration of their immunity.

According to the latest information, sixteen persons have been vaccinated against yellow fever in the Foundation's yellow fever laboratory in New York, and in addition three persons in Nigeria and Brazil have been immunized with material sent from this laboratory. Vaccination has so far been tried only on persons engaged in yellow fever laboratory or field work. The aim has been to give immediate protection to the small group of highly exposed workers. Immunization or protection is produced by a single injection of a dried mixture of yellow fever virus fixed for mice and human immune serum, with separate injections of additional serum to make up the amount required for protection. The immunizing substance can be shipped from the laboratory and used elsewhere, as was actually done in the three cases referred to above. The amount of serum required in vaccination varies as the body weight and seems to be independent of the virulence of the strain used.

The immunizing reaction after vaccination seems to be part of a true infectious process. So far as protective power is concerned, it has an effect similar to that of an attack of yellow fever. What we have now is a reasonably safe method of producing demonstrably active immunity in human beings. It has been shown in tests that the mixture of fixed virus and immune

serum retains its immunizing power for eight months when dried in a frozen state and sealed in glass.

The Rockefeller Foundation's research work on yellow fever is carried on in three laboratories; one of these is located in West Africa, at Lagos, Nigeria, another at Bahia, Brazil, and the third in New York City.

In addition to its laboratory and field research on yellow fever, the Foundation has from year to year been active in control work. During 1931 it assisted the government authorities of Brazil in extensive preventive operations against the disease.

Since most of the work for the control of yellow fever intimately touches the life habits of the mosquito, a considerable amount of effort has been directed toward increasing knowledge of the insect carrier of the disease. As was explained in the report of The Rockefeller Foundation for 1930, a number of mosquitoes other than *Aedes aegypti* have been found capable of transmitting yellow fever and may therefore enter the picture so far as control work is concerned.

During 1931 *Culex (Culex) thalassius* Theobald was definitely added to the incriminated list, and *Mansonia (Mansonioides) uniformis* Theobald was found to produce the disease when emulsified and injected subcutaneously into rhesus monkeys. Investigation of these species of mosquito was deemed important because they are abundant in certain sections of West Africa, because they enter houses, and because they bite man with great frequency.

Culex thalassius proved to be an inefficient vector in comparison with *Aedes aegypti*. However, the density of the species is known to be very great at certain places and this may compensate to some extent for its relative inefficiency, making it of some importance epidemiologically. *Mansonia uniformis* could not be kept alive in captivity long enough to demonstrate conclusively its ability to transmit yellow fever by biting, but compared with *Aedes aegypti* it also is not an efficient vector, although it may play a part in yellow fever epidemiology in places where the species is abundant.

The question of the effect of temperature on mosquito breeding is of importance in explaining the fact that yellow fever does not become endemic in certain parts of the world. At the Bahia laboratory experiments were performed on colonies of *Aedes aegypti* mosquitoes to determine the effect of different temperatures on their vital activities. It was found that at 36°C. the colony was unable to maintain itself in the second generation, the high temperature shortening the life of the adults, diminishing blood-sucking, and destroying fertility. At 19°C. conditions were apparently favourable. At 18°C. the mosquitoes did not feed well, but vital activities were continued at a pace adequate for the maintenance and even increase of the numerical strength of the colony.

In the literature dealing with the effect of cold weather in limiting the propagation and spread of yellow fever through failure of the mosquito host, attention has been directed chiefly to the adult stage of the insect and secondarily to the larval and pupal stages. Experiments to determine the effect of cold and heat upon fresh and matured stegomyia eggs were conducted at the Bahia laboratory. It was demonstrated that actual freezing kills practically all eggs of both types after relatively short exposure and that very high temperatures have an injurious effect, especially upon fresh eggs. Exposure to temperature of 40°C. to 45°C. killed stegomyia eggs rapidly. Matured eggs were slightly most resistant than fresh. In nature, unfortunately, probably the majority of eggs are deposited in-doors or in sheltered places where they are not subjected to extreme temperatures.

Another series of experiments in the laboratory in Bahia was devoted to determining whether modifications in temperature would affect the length of time required for incubation of infective yellow fever virus in *Aedes aegypti*. It appeared that the period was shortened at high temperatures and prolonged at low

temperatures. There was no loss of virulence in the virus even when the mosquitoes had been kept for four weeks at 8°C. and later subjected to 36°C. for six days.

From further experiments with *Aedes aegypti* in West Africa, it appears that the transfer of yellow fever virus from infected females to copulating males occurs in nature so infrequently that the possibility need not be considered as a factor in the perpetuation of the disease. This conclusion supports other evidence that yellow fever virus in infective quantities cannot be maintained indefinitely among mosquitoes without some suitable intermediary host.

The actual nature of yellow fever virus is as yet little known. There is doubt about its chemical composition, its physical structure, and even about whether it is alive or not. In a series of experiments, rabbits were inoculated repeatedly with active yellow fever virus contained in mosquitoes and in monkey serum. It was thought that if the rabbits developed precipitins against the virus, this would indicate that the virus is protein in character. However, the virus of yellow fever in mosquitoes was found to engender in rabbits neither precipitins nor protective bodies against the same virus contained in monkey blood. Large amounts of the virus from the blood of infected monkeys also failed to engender in rabbits demonstrable precipitins against the virus in mosquitoes. There were engendered in relatively small amounts protective bodies against monkey blood virus. It would seem that mosquito virus differs qualitatively from monkey blood virus in its power to engender protective bodies in rabbits. However, it cannot be said that definite conclusions are as yet warranted.

An attempt was made to throw light on the nature of the reaction by which yellow fever immune serum protects animals against infection. Electrophoresis experiments completed during the year indicate that the virus of yellow fever travels toward the negative pole in alkaline fluids and toward the positive pole in acid fluids. Yellow fever virus appears to travel with hæmoglobin regardless of charge and to be inactive in fluids that have more than certain degree of acidity.

The yellow fever virus is extremely labile and is changed or destroyed by the most minute and undetermined changes in the culture medium. But it is possible to grow the virus indefinitely in the laboratory in the presence of living tissues by methods successfully developed for other filtrable viruses.

The possibility of low fatality rates in natives of endemic or previously endemic areas must be taken into consideration in studying the distribution of yellow fever. In other words, the disease may occur quite generally in light form. A large part of the native population seems to be able to develop immunity without having the symptoms of the disease. This phenomenon is not limited to the black race. Some investigators suggest that this may be an hereditary immunity or at least an hereditary resistance. This would mean that the inhabitants of endemic areas are inheriting the protective mechanism.

Malaria

In West Africa an experiment was made to determine whether mass treatment with plasmochin, would be a practical antimalaria measure. Small doses of the drug were administered. Before this was done, in the spring of 1931, 1,350 mosquitoes of the locality were dissected and, among them, 4.6 per cent. were found infected. After the plasmochin had been administered 3,860 mosquitoes were dissected and only 0.4 per cent. were found to be infected, indicating a great drop in gametocyte carriers among the population. It seems as if the plasmochin treatment sterilized the human carriers, so that mosquitoes could no longer, in biting human beings, pick up and transmit the malaria organism. This particular study was made in a region where practically 100 per cent. of the children have malaria and where the parasite index of adults may be as high as 80 per cent. The anopheline density also is very high. Where

malaria is as prevalent as it is in this case, mosquito dissection furnishes a convenient means of measuring the results of control work. It would require additional and more extensive experiments to show whether mass treatment with plasmochin would be a practical means of malaria control in regions where the application of the usual antimosquito measures is for some reason either difficult or impossible.

Work was also done in connection with the technique of counting malaria parasites in the blood, with the aim of adapting this technique to field work and using it in areas where individuals are lightly infected. Other methods of malaria diagnosis are subject to various errors; and while it cannot be said that the counting of malaria parasites is an entirely accurate method, it has considerable value as a diagnostic technique.

Studies in Southern Nigeria, Africa, offered little evidence of any racial immunity to malaria. The degree of malaria infestation was found to be high at all ages up to middle life. Natives do not acquire complete tolerance to the effect of malaria parasites at least up to middle age.

In the Philippines, the habits and resting places of adult mosquitoes during the daytime were subjected to careful observation, with the aim of improving the technique of catching adult mosquitoes for the purpose of dissection and observation.

In India, in the state of Mysore, a great many mosquito dissections were carried out, but only a small number of mosquitoes were found to be infected with malaria. Such dissections come under the heading of routine laboratory work in connection with the control of malaria.

Hookworm and other intestinal diseases

In the course of the year there were published a number of papers dealing with medicaments for expelling the hookworm. This is a subject on which during the past fifteen years a great deal of research has been done. A number of fairly good vermifuges have been known for some time. But as new knowledge has been acquired, one drug after another has gradually been discarded in favour of something just a little better.

In a paper reviewing this entire subject, it is pointed out that because of the great differences in the structure and physiology of intestinal worms and in their location within the host, no one remedy can remove all types of these parasites. Chemotherapy, to be successful, must be based on a knowledge of the physiology and the life cycle of the various parasites. A recent study of all the substances that have been used in combating such intestinal inhabitants as *Ascaris*, *Trichuris*, *Enterobius*, and the hookworm has shown two of these to be safe and efficient anthelmintics, namely, tetrachlorethylene and hexylresorcinol, the former for uncomplicated hookworm infections, and the latter as an effective remedy also against certain parasites other than the hookworm.

A study was made of the effect of a deficient diet on the susceptibility of dogs and cats to hookworms other than those with which they were normally infected. These experiments suggest the possibility of a close relationship between undernourishment and incidental parasitism even in human beings.

One of the most important prophylactic measures in all hookworm work consists in the building and use of latrines. On this subject much information has been given in the early annual reports of The Rockefeller Foundation. It has been stressed that different kinds of sanitary conveniences are required in different parts of the world, in conformity with local habits, customs, and usages. In recent years considerable attention has been paid to a new device known as the bored-hole latrine, which is easily constructed and which offers certain other definite advantages.

During 1931, field studies of the effectiveness of the bored-hole latrine were conducted in the Philippine Islands; in the Province of Burma, the Madras Presidency, and the State of Mysore, in India; in Ceylon;

and in Egypt. In the United States such studies were a chief feature of the work at the research laboratory at Andalusia, Alabama. An article was published giving full information on bored-hole latrine equipment and construction.

Yaws

Mass treatment of persons with symptoms of yaws has been carried out, but this does not suffice to eradicate the disease. The reservoir of infection occurs among youths up to the age of seventeen, who give a history of yaws but show no signs of the disease. Treatment with salvarsan and similar drugs is causing the gradual disappearance of the disease in certain Polynesian groups. Recent progress in treatment has also been made in Melanesia.

Undulant fever

During 1931 individual cases of undulant fever were studied. In a survey of six communes, selected because of known prevalence of the disease, 12 per cent. of the entire population, or 14 per cent. of persons above the age of fifteen years, were found to have had the disease within the last five to seven years. Laboratory examinations supported epidemiological findings indicating goats and sheep as the main reservoir of infection. The most important means of human contamination seems to be contact with sheep and goats and their excretions. All cultures from human patients as well as from animals have been classified as *Brucella melitensis*. This disease constitutes a serious health hazard to human beings and produces great economic loss through abortion in animals.

Anæmia in Porto Rico

Various kinds of anæmia play an important rôle in the public health problem of Porto Rico. The types of anæmia associated with hookworm disease, malaria, and sprue are relatively common. During 1931 there was undertaken an investigation of selected cases of anæmia as possibly related to direct or indirect dietary deficiency.

In over 150 cases of anæmia associated with hookworm infestation, the rôle played by dietary deficiency and gastro-intestinal changes was clearly brought out. In a hundred cases of anæmia associated with sprue, there was found a close relationship between this disease and certain forms of pernicious anæmia. A careful study was made of the beneficial effect of various substances, especially liver extract, on the blood-forming organs of patients suffering from this form of anæmia.

[Note.—This abstract only deals with the work under the 'International Health division' of the Rockefeller Foundation. But in addition to this there is a long list of medical institutions under the 'Medical Sciences' section which receive grants in aid of specific researches. There are also sections dealing with 'Natural Science', 'Social Science', 'Humanities' the last including assistance to Libraries and Museums, but as these are not matters of strictly medical interest they have not been abstracted here.—*Error, I. M. G.*]

ANNUAL CLINICAL REPORT OF THE GOVERNMENT HOSPITAL FOR WOMEN AND CHILDREN, MADRAS, FOR THE YEAR 1931. MADRAS: PRINTED BY THE SUPERINTENDENT, GOVERNMENT PRESS. PRICE, RS. 4.

This annual report is always full of interest and the present one is doubly so far Lieut.-Col. Hingston has taken the opportunity, before relinquishing his post as superintendent, of giving a brief history of the institution since its inception. He is specially suited for this task as he has been in charge since the year 1914 and he is to be congratulated, for it is clear in the following abstract that the record of progress under his regime has been steady:—

The year 1931 was marked by an increased activity in all the departments of the hospital and was characterized by the fact that the largest number of deliveries

took place during the year since the inception of the hospital in 1844.

In consequence of the large numbers admitted, considerable strain was felt in arranging for accommodation and as unfortunately, owing to the financial crisis, some of the improvements that I had already foreshadowed in the previous report could not be carried out, there was chronic overcrowding in some sections of the hospital, particularly in the gynæcological, post-maternity and ante-natal sections.

This being the last annual clinical report that I shall have the privilege of submitting, I may perhaps be permitted to cast a glance backwards and review the position of the hospital as it is to-day, and to forecast what my hopes are for the future. This hospital was founded in September 1844, and by the end of that year, the total number of confinements was 15. In 1845, the first complete year of its existence, the total number of confinements was 62; in 1861 the number of confinements had just exceeded 1,000 and 30 years later, in 1931, the total number of confinements had just exceeded 2,000. When I took charge of the hospital in 1914, the total number of confinements was 2,251. It is a matter for gratification that the facilities afforded by this hospital have been increasingly utilized by the general public and as has been stated above, in this last year of my official connection, the total number of confinements has exceeded 3,350. This hospital owes a great deal to the enthusiasm and energy displayed by its successive superintendents notably by Harris, Branfoot, Sturmer and Giffard. It was during the time of Branfoot, in the year 1881, that the hospital was shifted to its present site, and the lay-out of this hospital, with its picturesque corridors and well ventilated, airy wards, is due to his sagacity and foresight. The next great change in the construction of the hospital was during the superintendentship of the late Sir Gerald Giffard, who was at the helm of affairs from 1906—1914. During his regime, important additions and alterations were made in the hospital, the most prominent of which were: the construction of the Giffard School, a separate block utilized only for purposes of teaching, fitted with a modern amphitheatre for lectures, rooms for museum specimens, clinical laboratories and research laboratories, a photographic department and residence for men and women students, so that they might have facilities of a stay in the hospital for definite periods for witnessing and conducting obstetric cases. Besides these improvements, the construction of the out-patient and office blocks in the front portion of the hospital, the building up of a wing known as the Branfoot block, wherein the section ward and the puerperal wards are accommodated; the structural alterations in the septic wing of the hospital; the construction of an operation theatre known as the 'Giffard Theatre'; the construction of a spacious Nurses' Quarters on the opposite side of the road in Halliburton's Gardens—these are some of the main additions and improvements for which he was responsible during his regime. It was fortunate that all this building programme was completed before the Great War began, and thus a great impetus was given to this hospital to go ahead with its main function as one of the largest teaching centres in obstetrics and gynæcology for midwives, medical students, and those who propose to take midwifery as a speciality.

During my term of office as superintendent, from 1914 to 1932, an additional theatre was constructed—the 'Hingston Theatre'; improvements were made in several of the wards; the kitchen and laundry were suitably altered and additions were made in the nurses' quarters for accommodation of Sisters, the English educated Indian midwives and the vernacular-trained midwives.

Much as has been the improvement effected during the last 25 years, I feel it my duty to state that this hospital, if it is to maintain its reputation and its status as one of the foremost obstetric centres in the British Empire, should keep pace with modern requirements, and it was with this view that I had already submitted proposals to the Government which I regret very much,

could not be taken up owing to the sudden financial stringency. It is my hope that as soon as the financial situation is relieved, the Government will be able to take up these very necessary improvements for the maintenance of the standards that have been set in this institution. Among the chief of these proposals to which I have referred in previous clinical reports are:—

The improvement of the labour ward with a view to equipping an obstetric operation theatre permanently where all obstetric cases requiring operative interference will be delivered under strict aseptic conditions and to the advantage of the large number of students and post-graduates who are anxious to witness such cases.

The improvement of the septic-delivery ward, which is now in an improvised portion of the hospital, is also urgent in my opinion. Plans have been submitted with a view to delivery of 'suspect' cases in separate cubicles and the obvious septic cases in other cubicles. I consider this is very essential to prevent any possibilities of cross-infection and to ensure the highest standards of aseptic midwifery to the women who seek relief at our hands.

The construction of an ante-natal ward and a suitable ante-natal out-patients' clinic, and a separate children's department, is also a necessity that should be taken up as early as possible. Within the last three years, we have organized more definitely an ante-natal out-patient clinic which is increasingly popular and which is in charge of a separate officer of the grade of a Civil Surgeon. The children's out-patient department has increased in utility, and I think it will soon be necessary to separate the infant welfare department from the children's clinic, and to concentrate more and more upon the physiological requirements of the infant through the infant welfare department.

The venereal disease clinic attached to the ante-natal clinic has also increased in its utility, while the out-patient gynaecological clinic is showing how much it can draw the patients from different parts of the country. It must be recognized that this hospital is not a hospital catering to the needs of the citizens of Madras, but is a provincial concern, and the majority of our serious cases, particularly gynaecological, and some obstetric cases, are drawn from practically every district of the Presidency and from the neighbouring Indian States. A hospital catering for the needs of such a large and diverse population should therefore be looked upon as a provincial concern, of utility to the citizens of the Presidency as a whole, and not to those of Madras in particular.

Within the last three years again, we have opened a Mothercraft Department which is now in charge of a trained Sister and this department has served not merely to look after those children who are entrusted to the care of the department, but to diffuse proper knowledge and information to many mothers in Madras who have freely resorted to the department for advice with regard to infant feeding and infant care in general. The department is also training a number of midwives in mothercraft work, so that when these midwives pass out, and go to the mofussil, they may carry the lighted lamp to many a dim corner where primitive ideas of infant feeding and infant care are now existent. All these activities have necessarily their own part to play in increasing the financial burden, but one may state with confidence that the returns for such expenditure as may have to be spent on the maintenance of an institution such as this, are immeasurably greater not merely in the health and safety of the mothers but also in the better conditions of life of the children and what is far more important, in the training of so many competent midwives and obstetricians, who I trust will disseminate this knowledge in their practice throughout the different parts of this Presidency and of India, in general. It has been a very gratifying feature for me to note that Indian practitioners are taking more largely to obstetrics and gynaecology and there has been a steady and an increasing stream of qualified practitioners

from all parts of India, from Burma, from Straits Settlements, Sumatra, Java and from several other parts of the Far East, for a post-graduate training in this hospital. The need for organizing such post-graduate training is great, and while every impetus has been given so far, I trust that in the future, a more systematized scheme of post-graduate training will be possible, when we have instituted our diploma of Licentiate in Gynaecology and Obstetrics, for which proposals have been submitted to the Government. The University, in 1927, instituted a Diploma in Gynaecology and Obstetrics, and I am glad to state that so far six graduates of the University have taken the Diploma. The Diploma in Gynaecology and Obstetrics, requires a course of study of one year, six months of which at least should have been spent as a House Surgeon in one of the recognized maternity institutions in the City, wherein the candidate would have conducted at least six cases of obstetric operative delivery under supervision; later a six months' training in the wards of this hospital is compulsory. I have submitted proposals to the Surgeon-General for the institution of a licence for those who are not in a position to take the longer course of a year, and it is contemplated that this licence may be of a six months' duration and that the course will be as practical as possible, so that the candidates who get through this course will have a very fair idea of the practice of obstetrics. I hope that in the future, the institution will be even more largely utilized for the post-graduate training of midwives, for I feel that it is no use our training midwives and sending them to the different parts of the country, if they are not given periodical post-graduate training, so that they may keep themselves up to the mark, and I can think of no institution which affords the same facilities for a short post-graduate training of three months for these midwives.

In-patients.

During the year 1931, 9,106 patients were treated in this hospital, of whom 947 were children and 8,159 were women and the following table gives the particulars regarding these admissions:—

	Admissions	Deaths
(1) Ante-natal cases ..	2,144	26
(2) Maternity cases (cases delivered in the hospital, or admitted within 24 hours after delivery at home) ..	3,389	84
(3) Post-maternity cases (delivered at home and admitted into hospital 24 hours after delivery) ..	228	28
(4) Children's section ..	947	188
(5) Gynaecological cases ..	1,360	37
(6) General diseases treated ..	1,038	43
TOTAL ..	9,106	406

The total number of deliveries for the year under report was 3,389, the total number of children born being 3,160, and the number of abortions being 270.

The total number of children delivered for the 3,119 women who were confined (exclusive of abortions) was 3,160. It will be noticed that the percentage of live-births was 91.04, inclusive of the macerated foetuses, and 93.8 exclusive of macerated foetuses. The greater proportion of still-births as compared with the rate of maternity institutions in the West is due to the fact that a heavy incidence of still-birth rate results in what are known as complex labours, that is, in those patients who come into labour with some complication of pregnancy, generally one of the tropical diseases. It is in these cases that prematurity is one cause of still-birth, and the complication itself the other main cause; and that this is so will be obvious from a study of the statement given above from which it will be

found that in the complex labours there were 73 macerated fetuses and 113 still-births.

It is in this class of labour also that neo-natal mortality is the largest and in the year under report, 97 children died among the complex labours. It is a great problem for the obstetrician how to avoid these complications in pregnancy in tropical countries like India, and one must confess that while ante-natal hygiene and ante-natal treatment will undoubtedly, if conducted on proper and sound lines, and pushed to the logical extent, mitigate the severity of these complications, the real problem will only be tackled when better hygienic facilities are available for the whole community. The incidence of malaria, typhoid, dysentery, influenza, the infectious fevers and pneumonias, is yet too great in the general community as well as in pregnant women to warrant the hope that the heavy morbidity and mortality both to mothers and children, can be reduced to any reasonable proportion, unless a much greater leeway is made with the general hygiene of the population at large. It does not however mean that ante-natal work should not be pushed forward with greater vigour than is apparently the case at present in the City as a whole. It only shows that brilliant or surprising results from ante-natal work alone cannot be expected unless the general hygiene of the population *pari passu* is improved.

An analysis of the causes of foetal mortality among the natural labours make it clear that the large majority of them were due to unavoidable causes so far as the hospital is concerned. There were 67 cases of tedious labour, with one macerated foetus, and 294 cases of laborious labour. Under 'laborious labour' the application of forceps was performed in 257 cases, while there were 4 cases of a symphysiotomy and 12 cases of Cæsarean section. Internal podalic version was performed in cephalic presentations in 15 cases, with 4 still-births, and no death to the mother. We may reiterate our experience that the delivery of a foetus as a breech presentation in those cases where, particularly in multiparæ, the head does not engage owing to an imperfect flexion or malposition, is far safer than the application of forceps, both to the mother and to the child.

There was one case of secondary abdominal pregnancy.

The statement below furnishes the details of complex labours. It will be noticed from this statement that there were—

	Cases
Plural births	41
Eclampsia	67
Accidental hæmorrhage	31
Placenta prævia	22
Rupture of uterus	8
Descent of funis	6
Post-partum hæmorrhage	48
Hydramnios	6
Foetal malformations	9
Albuminuria	100
Anæmia	115
Other complications	315
TOTAL	768

Puerperal eclampsia

There were 80 cases of eclampsia admitted for treatment during the year under report, of whom 14 died, giving a mortality of 17.50 per cent. Of the 80 cases, 43 were primiparæ and 37 multiparæ. During the year under report, there has been a change in the treatment of puerperal eclampsia. We still hold that the reduction of the blood pressure is one of the important things to look to, and we have attempted this by the administration of parathermone and calcium. Blood analysis has been made biochemically of a number of cases of eclampsia and a report on this condition as well as on the lines of treatment that are adopted is being submitted in a separate paper.

The details of the morbidity statement furnished makes it evident that the morbidity rates in tropical

countries must necessarily be much higher than in European countries. As a matter of fact, the very large number of cases of morbidity, whether it be in natural labours or in tedious and complex labours, are necessarily due not to the incidence of sepsis but to the various tropical complications which, as has been stated already, are far too frequent in pregnant women in tropical countries. Any useful comparison therefore is not possible as regards the standard of morbidity in maternity institutions in tropics and elsewhere.

In the gynæcological section of the hospital, 1,360 cases were admitted. We have during the last year under report, treated a very large number of cases of cancer of the cervix, the body of the uterus, and the vagina with radium therapy. Articles on this subject have been published by some of the members of the staff in medical journals and a concise report of the treatment of cancer with radium and of the results thereof will be published later. It is unfortunate that the large majority of cases come at a time when any possibility of operative treatment does not arise before or after radium treatment; and although radium has undoubtedly a very great effect upon improving the general health of the patient, relieving her of her symptoms notably pain and hæmorrhage and destroying large fungating growths, it cannot be said that the results have at all been satisfactory, taking a 3 or 5 year period test of survival into consideration. I can only hope that, with much better propaganda and a keener appreciation by the practitioners up-country of the early signs of cancer, we will be able to get into touch with these cases at a much earlier stage when either radium therapy by itself, or combined with operation, would prove much more satisfactory.

ANNUAL REPORT OF THE MEDICAL OFFICER OF HEALTH, OF COLOMBO, 1931. PRINTED AT THE MUNICIPAL PRINTING OFFICE, CEYLON.

We have on previous occasions commented on the excellence of these reports, which are well written, well printed and produced, and illustrated by good photographs and diagrams. The present one is of the same high standard. We believe that tourists have frequently noted the cleanliness of Ceylon; and this may be taken as an index of the care bestowed on less obvious matters of sanitation. Colombo has a population (1931) of 234,155. The birth rate for 1931 was 30.8, the death rate 25.1; the infantile mortality and maternal mortality rates 172 and 24.8 per 1,000 births. The chief point of note is the comparative absence of ordinary tropical diseases as causes of mortality, and the high incidence of phthisis (2.22 per 1,000), pneumonia (3.18 per 1,000) and diarrhœa and enteritis (1.56). The mortality from respiratory diseases is usually an index of bad housing and overcrowding. Parts of Colombo have over 150 persons per acre, and the average is 34 per acre. This is less than many of our Indian towns.

A very good description is given of the maternity and child welfare work. This is now on an excellent basis. The staff consists of one special whole-time medical officer, one Superintendent of Health Nurses, twenty-one Health Nurses and sixteen Midwives. Photographs of the dispensaries and welfare centres are given. The fact that the infantile mortality rate has diminished from 410 per 1,000 births in 1903 to 172 in 1931 is some testimony of what has been done. The maternal mortality, however, has not decreased in the same manner. In 1930, a Midwives' Ordinance was passed, which apparently insists on compulsory registration of every midwife; and such registration apparently depends on some form of training at least. The effect of this ordinance may emerge as time goes on, but cannot yet be judged.

Ever since 1913 plague has been endemic in Colombo, particularly in certain of the dock areas. There is a constant danger of exportation to the interior of the Island and indeed this has happened on several

occasions. Dr. Hirst's views on this are well known; i.e., that the beginning of plague in Colombo in 1913 was due to the importation and establishment of colonies of *Xenopsylla cheopis*. His views have been supported to a large extent by the investigations in Madras Presidency, of Lieut.-Col. King and his collaborators. In 1931 there were in Colombo 47 cases of human plague and 45 deaths. The earliest case was diagnosed as cerebral malaria and the second case was reported as primary pneumonic plague. No other pneumonic cases occurred however but only septicaemic and bubonic cases.

The phthisis problem was fully discussed in the previous report and is not revised again. It is in Colombo as in other towns in the tropics the health problem *par excellence*.

The report is well got up, easily read and informative.

Correspondence

VACCINATION AGAINST SMALLPOX

To the Editor, THE INDIAN MEDICAL GAZETTE.

SIR,—I shall be greatly obliged if you kindly give your opinion regarding the following points in connection with vaccination against smallpox.

Is it possible to fix any dose of the lymph to be inoculated?

The manufacturers of the lymph direct that a certain number of persons should be inoculated with the amount contained in the tube. We have recently found that more than 16 persons can be inoculated, apparently successfully, with a tube of lymph which was meant, on the manufacturers' word, only for 4 persons. There was the typical vesicle, pustule, and all that. Only a pin-point of lymph was used in most of these cases, and the scratches consisted only of one point.

Is the object of the vaccination simply to produce a sensitization of the system through the skin, or to give a definite dose, as in the case of ordinary vaccines, where so many millions of bacteria are introduced into the system?

If the object of vaccination be to sensitize the system through the skin, then why it is insisted that more than two places must be scratched in cases of primary vaccination, where the system is more likely to react, than in the case of the revaccinated, where the failure of some of the scratches may be expected?

If any particular dosage is advisable, then why is not stress laid on the length, breadth, and number of the scratches?

Yours, etc.,

A. B. MUKHERJI, L.M.P.

NUTANGUNJ,

BURDWAN,

22nd February, 1933.

[Note.—We referred the questions raised by Dr. Mukherji to Lieutenant-Colonel A. D. Stewart, I.M.S., Director, All-India Institute of Hygiene and Public Health, Calcutta, who kindly supplied the following information on the subject:—

'The questions put by your correspondent are of some importance and may interest the profession at large, especially in view of some of the recent vaccination orders by the Ministry of Health of England and Wales.

After the discovery of Jennerian vaccination against smallpox, the Germans took up the matter with characteristic thoroughness. They first demonstrated that the number of cases of smallpox developing after vaccination were very few indeed when there was evidence of four points of original vaccination, more numerous when there were three, and proportionately still more numerous when there were two, one, and none at all. They further showed that the protection was proportional

to the vesicular scar area (not necessarily the whole scar area); the typical vesicular area being the foveal spot with a central spot of umbilication. They finally showed that the maximum amount of protection was procured when at the primary vaccination a certain minimum amount of vesicular area was produced. This was found to be half a square inch. When less than this area was produced, the protection was not maximal, but a vesicular area in excess of this did not increase the protection given. Efficient vaccination was then defined as resulting in "the maximum amount of protection at one vaccination, with the minimum amount of trauma". This last condition was satisfied if the vesicular area was spaced over four insertions in the form of simple linear incisions about half an inch long. To obtain fully efficient primary vaccination, therefore, a certain amount of lymph, sufficient for the four incisions, is necessary. It is this amount of lymph which is referred to as being necessary for one person and which forms the basis of calculation and instruction for use by vaccine departments. A certain amount of protection can be given with one insertion, but it is not maximal and lasts for a shorter period. The question whether this maximal protection is always necessary has been raised by the Andrewes and the Rolleston commissions on post-vaccinal encephalitis (see *Indian Medical Gazette*, August 1930, p. 459 for a good résumé of this subject). "One-point" vaccination with diluted lymph is now recommended in many cases, with revaccination at shorter intervals. Post-vaccinal encephalitis about the year 1922 was more frequent in Holland and England than elsewhere and it was found to occur practically only in primary vaccinations in older children (3 to 12 years) and practically not at all in infancy. One doubtful case only has been reported in India (see *Indian Medical Gazette*, August 1930, p. 443). Infancy is therefore the best period for primary vaccination and in India I see no reason at present for not trying to get the full efficient vaccination with four points.

Cross-hatching methods of vaccination should be absolutely forbidden of course (it is yet distressingly common). Simple linear incisions are satisfactory or the circular drill, used carefully, inflicts little damage.

I think these observations may meet your correspondent's queries.—EDITOR, *I. M. G.*

Service Notes

APPOINTMENTS AND TRANSFERS

THE services of Lieutenant-Colonel T. L. Bomford are replaced at the disposal of the Government of India, Army Department, with effect from the 26th February, 1933, on the expiry of the leave granted to him.

Lieutenant-Colonel P. F. Gow, D.S.O., officiating Second Professor of Midwifery, Medical College, Calcutta, is appointed as Professor of Midwifery of the College and Obstetric Physician and Surgeon, Medical College Hospitals, *vice* Lieutenant-Colonel V. B. Green Armytage, granted leave.

Lieutenant-Colonel W. J. Powell, C.I.E., Inspector-General of Prisons, Central Provinces, is appointed to officiate as Inspector-General of Civil Hospitals, Central Provinces, during the absence of Colonel Wilson on leave.

Major B. G. Mallya is appointed temporarily as Superintendent, Campbell Medical School and Hospital, Calcutta, with effect from the 9th February, 1933.

Major L. K. Ledger, an Agency Surgeon on return from leave, is posted as Agency Surgeon, Gilgit, with effect from the forenoon of 15th October, 1932.

The services of the undermentioned officers are placed permanently at the disposal of the Government of the Central Provinces, with effect from the dates shown against their names:—

Major J. M. R. Hennessy, 2nd September, 1931.

Major R. A. Logan, 19th April, 1932.

The services of Major S. L. Patney, are placed permanently at the disposal of the Government of Bengal, with effect from the 11th July, 1930, for employment in the Bengal Jail Department.

The services of Major S. D. S. Greval, an officer of the Medical Research Department, are placed temporarily at the disposal of the Government of Bombay for appointment as officiating Assistant Director, Haffkine Institute, Bombay, with effect from the 14th November, 1932.

The services of Captain H. S. Waters are placed temporarily at the disposal of the Government of Bombay, with effect from the forenoon of the 5th December, 1932.

The services of Captain J. J. Beausang are replaced at the disposal of His Excellency the Commander-in-Chief in India, with effect from the forenoon of the 4th February, 1933.

Captain G. F. Taylor, an Officiating Agency Surgeon, on return from leave, is posted as Medical Officer and *ex-officio* Vice-Consul, Sistan, with effect from the forenoon of the 4th February, 1933.

The undermentioned officer is confirmed in the rank of Captain:—

Captain (provl.) F. H. A. L. Davidson.

PROMOTIONS

Lieutenant-Colonel to be Colonel

Brevet-Colonel E. C. Hodgson, D.S.O., K.N.P. Dated 23rd January, 1933, with seniority 30th July, 1927.

Majors to be Lieutenant-Colonels

N. K. Bal, M.C. Dated 25th January, 1933.

H. S. G. Haji, M.C. Dated 25th January, 1933.

S. S. Sokhey. Dated 26th January, 1933.

J. Findlay. Dated 26th January, 1933.

W. C. Spackman. Dated 26th January, 1933.

J. C. De. Dated 26th January, 1933.

C. H. P. Allen. Dated 26th January, 1933.

R. V. Martin. Dated 26th January, 1933.

The promotion of Major J. J. Rooney to the rank of Major is antedated to the 22nd January, 1929.

Captain to be Major

J. A. W. Edden. Dated 20th January, 1933.

The provisional promotion to the rank of Captain of the undermentioned officer is confirmed:—

Captain (on prob.) (provl.) Sangham Lal.

Lieutenant to be Captain (provl.)

G. K. Graham. Dated 3rd February, 1933.

The seniority of Lieutenant (on prob.) J. W. Bowden is antedated to 20th October, 1931.

LEAVE

Colonel H. R. Nutt, Inspector-General of Civil Hospitals, United Provinces, is granted leave on average pay for 7 months, and 5 days, with effect from the 30th March, 1933.

Colonel F. E. Wilson, Inspector-General of Civil Hospitals, Central Provinces, is granted leave on average pay for 3 months and 16 days combined with leave on half average pay for 4 months and 15 days, with effect from the 7th March, 1933, or subsequent date from which he may avail himself of it.

Lieutenant-Colonel E. W. O'G. Kirwan, Professor of Ophthalmic Surgery, Medical College, Calcutta, and Ophthalmic Surgeon, Medical College Hospitals, is granted leave for 8 months, with effect from the 25th February, 1933, or date of availing.

Lieutenant-Colonel H. Hingston, Surgeon to His Excellency the Governor of Bengal, is granted leave for 28 months from the 9th March, 1933, or any subsequent date of availing.

Lieutenant-Colonel V. B. Green-Armytage, Professor of Midwifery, Medical College, Calcutta, is granted leave for 2 years and 4 months from 27th March, 1933.

or from any subsequent date on which he may be relieved.

Lieutenant-Colonel J. B. Lapsley, M.C., Officer in charge Medical Store Depot, Lahore Cantonment, is granted 12 months combined leave ex-India (the first two months being privilege leave), with effect from the 5th June, 1933, or date of availing.

Lieutenant-Colonel G. G. Hirst, Officer in charge Medical Store Depot, Madras, is granted privilege leave from the 1st April to 31st May, 1933, combined with leave on private affairs ex-India from the 1st June, 1933, to 23rd January, 1934, pending retirement.

Major A. H. Harty is granted 8 months' leave, with effect from the 1st March, 1933, or subsequent date of relief.

Major S. N. Mukherji, Superintendent, Campbell Medical School and Hospital, Calcutta, is allowed leave for 1 month, with effect from the 27th January, 1933.

Major H. Williamson, O.B.E., an Agency Surgeon, is granted under Fundamental Rules, leave for 1 month, with effect from 16th January, 1933.

Major W. P. Hogg, D.S.O., M.C., an Agency Surgeon, is granted leave for 6 months, with effect from the forenoon of 15th October, 1932.

RETIREMENT

Lieutenant-Colonel M. R. C. MacWatters, retires with effect from 4th January, 1933.

Notes

EPHEDROL

THIS new cold cure, which is put up in a very convenient form, has a composition as follows:—

R. Ephedrine	1 per cent.
Camphor.	
Menthol aa	2 per cent.
Aromatic oil	q.s.
Neutral oily base to 100 parts.			

The chief difficulty which has attended the use of such solutions in the past has been the trouble encountered by the patient using an atomiser which is expensive, and quickly gets out of order. Ointments in tubes are unsatisfactory as the medicament does not penetrate far enough into the nasal passages to be of much use.

Ephedrol is packed in one ounce bottles with a special orifice designed to fit the nostril. The flat-shaped bottle is ideal for carrying about, and enables the patient to use it at the first symptoms of nasal catarrh or hay fever.

KODAK LTD.

THE value of the cinema as an aid to medical education and as a medium in health propaganda is daily becoming more apparent. Kodak Ltd. are therefore doing all those interested in health propaganda, as well as those with a more general interest in the cinema, a singular service in arranging for the employment of a cinema expert with a world-wide reputation to be available in India. Mr. G. Quiribet has just arrived in India to join the staff of Kodak Ltd. in Bombay.

Mr. Quiribet's name is already famous in two continents, where he has assisted in the production of a number of pictures. He has seen the cinema industry evolve from small, obscure beginnings to one of the first magnitude, his experience dating back to 1906, when he was in charge of one of the laboratories of Pathé Frères Producing Co. Later he went to England and after the war realising that America was introducing revolutionary improvements and rapidly perfecting film

technique, he went over and worked in two of the largest American studios.

It is hoped that Mr. Quiribet's valuable experience will aid the cinema industry in India, and lead to the production of pictures of educative and artistic value equal to those which are now imported from other countries.

UPPER FIXATION FORCEPS

By D. PRIESTLEY SMITH, M.B., M.R.C.S.

These forceps are for fixing the eye in cataract extraction. One foot is placed on the upper limbus and the other 5 or 6 mm. higher up on the globe. They



are then closed. This gathers up the intervening conjunctiva to the limbus, where it forms a fold or pleat held at its base in the forceps. This affords very good fixation. The corneo-scleral section is now made forthwith, the knife cutting out immediately behind the feet of the forceps, i.e., through the posterior layer of the conjunctival fold. This procedure makes a good conjunctival flap. The forceps are made by Down Bros. Ltd., London.

HALIVEROL

VITAMIN THERAPY IN TUBERCULOSIS

THERE appears to be an increasing interest in the possibility of favourably influencing tuberculosis by vitamin-D therapy, and growing opinion that adequate doses of vitamin D are of value in promoting calcification of tuberculous lesions. The use of vitamin D for this purpose has an obvious rationale.

The calcification of the tubercle has long been considered as one of the end results of the constructive forces in the healing of tuberculous infection in tissue. Obviously, therefore, therapeutic measures which tend to increase calcification might be regarded as logical.

Crimm (*American Review of Tuberculosis*, January-June, 1931) reported that 'the use of activated ergosterol in therapeutic doses increased the absorption of calcium and inorganic phosphorus', and stated, in relation to the use of irradiated ergosterol in the treatment of pulmonary tuberculosis, 'In the end it may prove to be more effective in the acute disease than sunshine is in chronic pulmonary tuberculosis'.

The above and other reports indicate a growing interest in vitamin-D therapy in the treatment of pulmonary tuberculosis.

It is therefore apparent that if cod-liver oil and irradiated ergosterol have a beneficial effect in this condition that other substances which are richer in vitamin content may be expected to give equally good, if not better, results. Haliverol (Parke, Davis & Co.) for example is said to contain 60 and 250 times as much vitamin A and D, respectively, as does an equal quantity of cod-liver oil and should be particularly useful.

Gordon and Flanders (*American Review of Tuberculosis*, 1931) have emphasized the importance of maintaining adequate vitamin-A intake in tuberculous patients. The many physicians who have had long-continued and firm faith in cod-liver oil in the treatment of tuberculous patients, because of it affording both the fat-soluble vitamins, will welcome the advent of Haliverol. Many tuberculous patients have a capricious appetite and cod-liver oil is obnoxious to them. Others have a limited digestive capacity for fats. While fat is an essential part of the diet for the tuberculous patient, this can be more advantageously provided by

butler and cream. The chief justification for the use of cod-liver oil in tuberculous patients is as a vehicle for the fat-soluble vitamins. This can now be provided in larger doses and much more conveniently in Haliverol.

In addition to Haliverol in liquid form convenient capsules are now available; they are easily swallowed and are of 3 minims capacity, i.e., they contain the equivalent of three teaspoonfuls of the finest cod-liver oil in vitamin A and 3 minims of irradiated ergosterol 250 D in vitamin D. The standard package contains 25 such capsules, and for small children and others unable to swallow a capsule the liquid is available in vials of 5 c.cm. and 50 c.cm. in cartons, with convenient

droppers included—9 drops from which equal the contents of a capsule.

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Original Articles

SOME BYPATHS OF ORTHOPÆDIC SURGERY

By W. L. HARNETT, M.A., M.D. (Cantab.),
F.R.C.S. (Eng.)

LIEUTENANT-COLONEL, I.M.S.

*Professor of Surgery, Medical College, Calcutta, and
Surgeon to the College Hospitals*

No country offers a wider field for the orthopædic surgeon than India. Fractures and dislocations occurring in villages far from medical aid are undiagnosed and are treated by the most primitive methods, with the result that months afterwards surgeons see them with the most astonishing deformities, for the treatment of which the textbooks give one little help. Inflamed joints are allowed to lie for months in the position most comfortable to the patient, who presents himself with extreme degrees of flexion or abduction, such as are never seen in Europe and which tax all one's resources to rectify within a reasonable time and obtain a good functional result. These are the common cases, but amongst them the rarer orthopædic conditions will be met with from time to time if one is on the look-out and it is with some of these that this paper deals.

Little's disease

Case I.—The patient, admitted to the Prince of Wales' Hospital on 18th December, 1930, was a Bengali boy, aged 8. The parents were healthy and he was the fourth child; the first child was born dead at 7 months, the second was a still-birth at full term, the third, also a full-term child, died a few hours after birth, and the patient had been a full-term child. All the labours were prolonged, but there was no history of instrumentation; all the labours were conducted by *daïs*. The parents denied the possibility of syphilitic infection. From birth it was noticed that the child kept his hands and legs crossed, but the deformities of the legs were not noticed until he was about four months old and those of the hands at a later date. It was also stated that there was sometimes defective control of the anal sphincter. The child began to walk later than usual and always with difficulty. Mentally the boy has always been intelligent and in advance of his years, but of a somewhat unstable temperament. On examination he was found to be well developed but rather thin. The thoracic and abdominal organs were healthy, the urine and faeces were normal and there was no fever. Both legs were adducted and internally rotated at the hip joints, and both feet were in marked equino-varus with adduction of the anterior parts of the feet; all these changes were more marked on the right side than on the left, and callosities had formed over the talus on both sides from walking on the outer borders of the feet. Spasticity of the tibialis anticus and tibialis posticus muscles was very marked, so that eversion of the feet was impossible and any attempt to produce it forcibly set up spasm and pain. The knee joints were held in the extended position and could be easily flexed, but extension was resisted by spasticity of the flexor muscles. There was a normal range of unresisted flexion and extension at the hip joints, but abduction was checked by spasm of the adductors; all these changes were more marked on the right

side. In walking there was marked adduction of the thighs, producing a tendency to cross-legged gait which the patient resisted by an effort of will, whilst the internal rotation of the feet necessitated the legs being held wide apart. The joints of the upper limbs had a normal range of movement, except for pronation of the right forearm, which could not be corrected. By gentle steady pressure the spastic muscles of the lower limb could be stretched until the foot was in a normal position, but the manœuvre was apt to set up clonic spasms and the deformity reappeared as soon as the pressure was relaxed. The knee jerks were exaggerated and ankle clonus was present on the right side, but patellar clonus was not present. Sensation was normal and there was no muscular wasting. The boy was intelligent and very anxious to overcome his disability, but was of an excitable nervous disposition. The Wassermann reaction was negative.

This disease is a lesion of the upper motor neurone due to disease or injury of the cerebral motor centres, resulting in a condition of muscle hypertonicity with exaggerated reflexes. It is not therefore strictly a paralysis, but a hypertonicity varying from slight muscular irritability to a condition of spastic rigidity which renders the limbs useless, not from loss of muscular power but from excess of contraction. According to its distribution it may be a monoplegia, diplegia, hemiplegia or paraplegia.

The causes may be ante-natal, natal, or post-natal:—

Ante-natal cases are due to errors in development and syphilis is an occasional factor.

Natal cases include the majority. Intracranial hæmorrhage is caused by trauma to the head during prolonged labour, forceps delivery or prolonged asphyxia at birth, leading to sclerosis, cysts, atrophy and porencephaly affecting the cortex, corpus striatum and basal ganglia.

Post-natal cases are mostly due to chronic meningitis, encephalitis and polio-encephalitis, or thrombosis due to marasmic conditions or to syphilis.

However it be caused, the essential pathology is a lesion of the motor area with atrophy of the affected portion and degeneration of the pyramidal tracts and two-thirds of the cases occur during the first three years of life.

The clinical signs will of course vary with the type of case; but a stiff irritable condition of the muscles is common to all, any effect at control of the limb or the execution of a special movement being apt to throw them into increased spasm. Standing, walking and all movements are executed clumsily and uncertainly, the impression produced being that the muscles have taken charge and that the patient is making efforts of volition to control them, which is exactly what is taking place. The limbs tend to assume certain positions determined by the relative strength of the opposing groups of muscles, the foot is held in equinus with often an element of varus or valgus, the knee is flexed, and the hip is flexed, internally rotated, and adducted. If both limbs are affected by adductor spasm the patient will cross one leg over the other when an attempt

is made to walk (scissors gait). In the upper limb the shoulder is held internally rotated and adducted with the elbow flexed, the forearm pronated and the fingers flexed. At first these deformities can be corrected by manipulation, though the sustained pressure often sends the whole limb into generalized spasms, later adaptive muscular shortening occurs and the deformities cannot be corrected, an important point to be considered in determining the line of treatment. Increased knee jerk, ankle clonus and other signs of loss of control by the upper motor neurone are present in varying degree, according to the severity of the case, choreic and athetoid movements occur in the paralysed limbs in the worst cases. In the majority of cases some degree of mental impairment exists, varying from practical idiocy to a defect which may be so slight that it is only manifested as the child grows older and becomes sensible of the limitations imposed by his condition. Mental deficiency to such a degree that the child is unable to understand and obey orders is an absolute bar to surgical treatment, since the child will be unable to co-operate in the all-important re-education of the muscles.

The case described above was a good example of a mild type of the disease. The attitude of the feet was characteristic, but the knee joint position was atypical in being held in extension rather than in flexion. The hip showed adduction deformity sufficiently severe to cause a mild degree of cross-legged progression, but no flexion. The upper limbs were normal except for spasticity of the pronators of the right forearm. The child was very bright mentally and anxious to improve, so that he was as favourable a subject for treatment as one would be likely to meet. These cases are not at all uncommon in India, no matter for surprise when one considers the ætiology, though usually they suffer from such a degree of mental impairment that their condition is hopeless. When this is not the case, as in the present instance, a great deal can be done by surgical treatment. The lines of treatment fall into two groups of methods:—

A. Non-operative treatment

Muscle re-education is an essential part of the after-treatment of operated cases, though by itself it is not enough except in the mildest cases. It aims at teaching the patient to use the weaker muscles, the instructor carrying the movements a little beyond the extreme range of voluntary movement by gentle stretching, the effect of which is a gradual increase in the range. Non-weight-bearing exercises are of course preferable and rhythmical movements such as drill are of great value. Only a minority of cases can be handled by these methods alone. Where marked muscular resistance is encountered in performing the exercises operative measures are desirable if the intelligence of the patient is such that post-operative

muscle re-education seems practicable. Massage is contra-indicated in this condition, as it increases muscular tone, and intermittent stretching of the contracted muscles tends to make them stronger and the muscular balance worse than it was originally. Continuous stretching on the other hand is good treatment, provided that it does not set up spasm which means that it must not be increased beyond the position of easy tolerance.

B. Operative treatment

This should not be attempted before the age of 5 or 6 years and then only in children with sufficient intelligence to understand and obey orders. The operations employed may be classified as follows:—

1. Operations on the peripheral nerves

(a) *Foerster's operation of intraspinal section of the posterior spinal nerve roots proximal to their ganglia.*—It was hoped that this operation by cutting the afferent paths to the cord would check the hyper-activity of the muscles deprived of the controlling influence normally exercised by the pyramidal tracts. The results of this severe operation were disappointing, as it was found that voluntary control was diminished no less than reflex spasticity and the operation has now been abandoned in favour of simpler methods.

(b) *Sympathetic ramisection.*—Hunter believed that muscle tone was largely under the influence of the sympathetic system and that the operation of ramisection devised by him and Royle would abolish spasm whilst leaving voluntary control intact. That some degree of success has been attained by this operation is undeniable, but a committee of orthopædic surgeons in London who examined the end-results of a series of cases operated upon by Royle himself reported that the results were not permanent and the operation is not likely to come into general use, though it has blazed the trail for operations on the sympathetic system in other conditions which do not concern us here, but which appear to be opening up a new and promising branch of neuro-surgery.

(c) *Stöffel's operation* interrupts the reflex arc on the motor side. By studying the intraneural topography of the large nerve trunks, Stöffel demonstrated that the various tracts run independently for a considerable distance and that the position of any bundle in a large nerve at a given level is remarkably constant. He was therefore able to pick out the nerve supply to any required muscle group and destroy as much or as little as he wished in any individual case. This relaxed the spasm in a certain number of muscle fibres in each muscle by cutting out part of its nerve supply. Stöffel's operation is not now used in its original form, surgeons preferring to follow the nerve down till the branches to the individual muscles can be traced. The whole or a portion of the nerve

supply to a given muscle is resected and in this form the operation has become firmly established, the effect is lasting and there is no tendency to recurrence. Its most successful application is in the ease of the adductor spasm by resection of the anterior branch of the obturator nerve or in severe cases of the whole nerve. It can also be applied to the sciatic nerve for the treatment of knee flexion, to the tibial and superficial peroneal nerves for pes equinus and lateral deformities of the foot and to the median nerve for the correction of contracture of the pronator radii teres and of the flexors of the fingers.

2. Operations on muscles and tendons

These include tenotomy, myotomy, tendon lengthening, tendon transplantation and shifting attachments of muscles. These are the oldest forms of treatment and are of great value, but all have the drawback that they do not attack the underlying causes of the condition, the diffuse irregular efferent nerve impulses which produce the spasm, so that recurrence of the deformity is very likely to occur. It must also be borne in mind that spastic muscles bear stretching very badly, the attempt to do so often causing marked general disturbance, an increase in the nervous symptoms and even convulsions, so that it is never wise to put up limbs in a more corrected position than the gain by operation easily permits. Nevertheless much can be done by these comparatively simple methods and in general it may be said that whilst the milder cases will yield to peripheral operations, the more severe call for Stöffel's operations on the motor nerves supplemented by peripheral tenotomies, etc., to correct any real contractures which may have developed. In any case the subsequent treatment by muscle re-education is to be regarded as the most important part of the regime, to which operation merely removes the obstacles.

The case described was treated as follows:—

1st stage.—Manipulation under general anaesthesia. All the deformities disappeared as soon as the patient was under the anaesthetic, and no fixed contractures were found; he was put up in plaster of Paris with the thighs fairly widely separated. This treatment caused great pain and spasm and for many days he had to be kept under the influence of sedatives. As soon as the plaster splint was cut off, the deformities all reappeared, not the slightest benefit having resulted.

2nd stage.—One month later, Stöffel's operation on the anterior branch of the obturator nerve of the right side.

3rd stage.—Two weeks later, Stöffel's operation on the left obturator. The benefit derived from these operations very soon became apparent and after a few months of exercises designed to stretch the remaining adductor muscles the boy was able to abduct his thighs freely, though not yet to the normal degree.

4th stage.—Six months later, Stöffel's operation on the right posterior tibial nerve. A long incision was made directly downwards in the midline from the centre of the popliteal space. The tibial nerve was identified and followed down by splitting the gastrocnemius and soleus muscles. By electrical stimulation the nerves to the medial and lateral heads of the gastrocnemius and that to the tibialis posterior were identified and divided, the branch to the flexor longus hallucis which arose in common with the branch to the tibialis posterior being also divided. The dissection necessary is a somewhat formidable proceeding, but the use of a tourniquet much facilitates the operation. The writer then went on long leave out of India and the patient was discharged one month later; the note on discharge records that the wound was completely healed, that there was good abduction, the cross-legged progression had completely disappeared and that the spasm of the leg muscles was much less.

The patient was seen again one year later and the improvement in his condition was most gratifying. The knee jerks were still exaggerated, but the ankle clonus had disappeared. There was still slight flexor spasm resisting full extension of the knees especially on the right side, though the knees were held in extension in walking. Abduction of both hips was quite free and there was no tendency whatever to adductor spasm in walking. There was practically no equinus and only slight varus on the left side, but on the right side there was a good deal of equinus, marked varus and marked internal rotation of the whole limb; all these deformities could be corrected by firm sustained pressure without setting up spasm. The pronator deformity of the right forearm was fixed and could not be corrected; on the left the forearm could be supinated almost to the full. The gait was enormously improved, but the internal rotation of the right leg caused the boy to walk with his feet wide apart. This result is most satisfactory but much further work remains to be done, which must take the form of peripheral operations.

The programme outlined for this patient on readmission to hospital is as follows:—

(1) Shifting the attachments of the gluteus medius and tensor fasciæ femoris lower down the ilium (Jones' operation), or section of the superior gluteal nerves on the right side.

(2) Lengthening of the tendons of the tibialis anterior and posterior on the right side.

(3) Detaching the insertion of the right pronator radii teres and transplanting it into the extensor carpi radialis longior.

Figure 1 is a photograph of this boy after the obturator nerves had been sectioned, but before the operations on the posterior tibial nerves.

Figure 2 is of a case recently admitted, showing the typical deformities of both upper and lower limbs. The photograph shows the attitude assumed during walking and is a good example

of cross-legged progression. This child, aged 12, is very intelligent and therefore a good subject for operation. A bilateral Stöffel on the anterior branches of the obturator nerves has been performed and the legs put up in plaster in abduction; at operation a certain amount of organic contracture was demonstrated and if this cannot be overcome by simple stretching the next stage will be a tenotomy of the adductor longus tendon on both sides, as it is essential that the adductor spasm be overcome before any attempt is made to tackle the deformities of the feet, the marked valgus in this case is secondary to the adduction and will tend to disappear when the normal line of weight-bearing is restored.

Two obturator neurectomies have also been done in infants with excellent immediate results in that the adductor spasm was completely corrected, but it is impossible to forecast the ultimate results and unless the after-care is intelligently carried out relapse is quite likely. The operation is difficult in infants on account of the small size of the nerves and the difficulty of identifying them in the abundant fat which lies between the muscles, but the advantage of early operation lies in the prevention of the development of permanent contracture, which is certain to occur in severe cases.

Osgood-Schlatter disease

Case II.—The patient, A. C., was an Anglo-Indian boy, aged 14½ years. His father died of pulmonary tuberculosis and a younger brother suffers from glandular tuberculosis. This boy has always been healthy except for infantile ailments. He is at school and takes part in all games and sports with great vigour. Six months ago he began to suffer from slight pain below the knee joints brought on by exercise and four months ago slight tender swellings appeared below the knee joints, which were painful after exercise and in the evenings, but better in the mornings after a night's rest. Rest always alleviated the pain and he never had any 'starting pains'. The condition is getting steadily worse.

On examination the tibial tuberosities were found to be slightly swollen and tender on pressure, but not reddened and there was no evidence of fluid in the swellings. The knee joints were perfectly normal, there was no limitation of movement, but there was pain over the tibial tuberosities on extreme flexion and on sharp extension. There was no limp in walking.

The radiogram (figure 3) shows the epiphysis of the tibial tubercle slightly separated from the underlying tibia, its lower edge broken off and the outlines slightly hazy. Both legs showed the same condition, which is a typical example of the disease described by Osgood in 1903 and by Schlatter a few months later. The tuberosity of the tibia arises from a tongue-like projection from the upper epiphysis with a separate centre of ossification. True partial separation of the tuberosity from trauma such as violent contraction of the quadriceps muscle occurs mostly in males of 16 to 18 and is unilateral. Osgood-Schlatter disease occurs at an earlier age, from 13 to 15, and though injury is to some extent an exciting factor, the symptoms come on insidiously and a clear history of injury or strain is unobtainable, as in the present case. Both knees are usually affected, the tubercle is enlarged and tender and pain is complained of after exercise, increased by full voluntary extension, since the epiphysis is pulled on by the contracted quadriceps muscle and

by passive complete flexion, as the epiphysis is then dragged upon by the stretched quadriceps.

The prognosis is excellent if the quadriceps muscle is thrown out of action for a time, allowing the epiphysis to settle down on the tibia again and the inflammation to subside. In the present case plaster-of-Paris knee caps were fitted to both knees for two months, after removal the knees were exercised daily for a month without weight-bearing and the patient was discharged free from symptoms. In some chronic cases it is desirable to limit knee flexion for about six months by fitting a knee cage with a stop allowing only 30° of flexion. No operation is ever necessary.

Osteo-chondritis of the hip: Legg-Perthes' disease

Case III.—E. B., Anglo-Indian boy, aged 12. Complained of difficulty in walking for six months and lately shortening of the right leg had been noticed. The onset was insidious, there was no definite history of trauma, merely a gradual development of a slight limp. There had never been any fever and there was nothing of importance to note in the previous history.

On inspection the right leg showed slight apparent shortening, amounting to ½ inch. The right great trochanter was more prominent than the left and there was a slight appearance of fullness in Scarpa's triangle. There was lumbar lordosis and when Thomas' test was applied by fully flexing the left hip joint it was found that the right hip joint was held flexed to 20°, it could be fully flexed, but extension was checked by muscle spasm. The right hip joint was adducted and only a slight degree of abduction was possible, the pelvis was raised on the right side to compensate the adduction, thus causing the apparent shortening. There was no real shortening and the trochanter was not raised above Nelaton's line. Rotation, especially internal rotation, was slightly limited. None of these movements caused pain unless an attempt was made to overcome the muscular spasm which was holding the joint in the abnormal position. The right thigh was slightly wasted. Walking was painless, but the patient limped on account of the flexed attitude of the joint and the limited movement. The left leg was quite normal. The radiogram (figure 4) showed the characteristic changes of the disease—a thin, sclerosed and fragmented epiphysis for the head of the right femur and thickening of the neck with bony absorption below the epiphyseal line.

This disease belongs to a class of affections of the epiphyses the ætiology of which has not yet been satisfactorily explained. In each country the disease is known by the name of the surgeon who first described it, so that different countries call them by different names, thus we have the names of Legg, Calvé and Perthes attached to this disease, though it was first described by Legg of Baltimore. Köhler's disease of the tarsal navicular, Köhler-Freiburg disease of the 2nd meta-tarsal, Keinboch and Preiser's osteoporosis of the carpal bones, epiphysitis of the vertebrae and of the calcaneus and several others are all probably of the same nature. The controversy turns on whether these conditions are of traumatic or inflammatory origin. Since these cases never terminate fatally and operation is not often indicated, there have been few opportunities for bacteriological and histological studies, the only points on which all writers

PLATE V



Fig. 1.



Fig. 3.



Fig. 2.



Fig. 4.



Fig. 5.



Fig. 7.

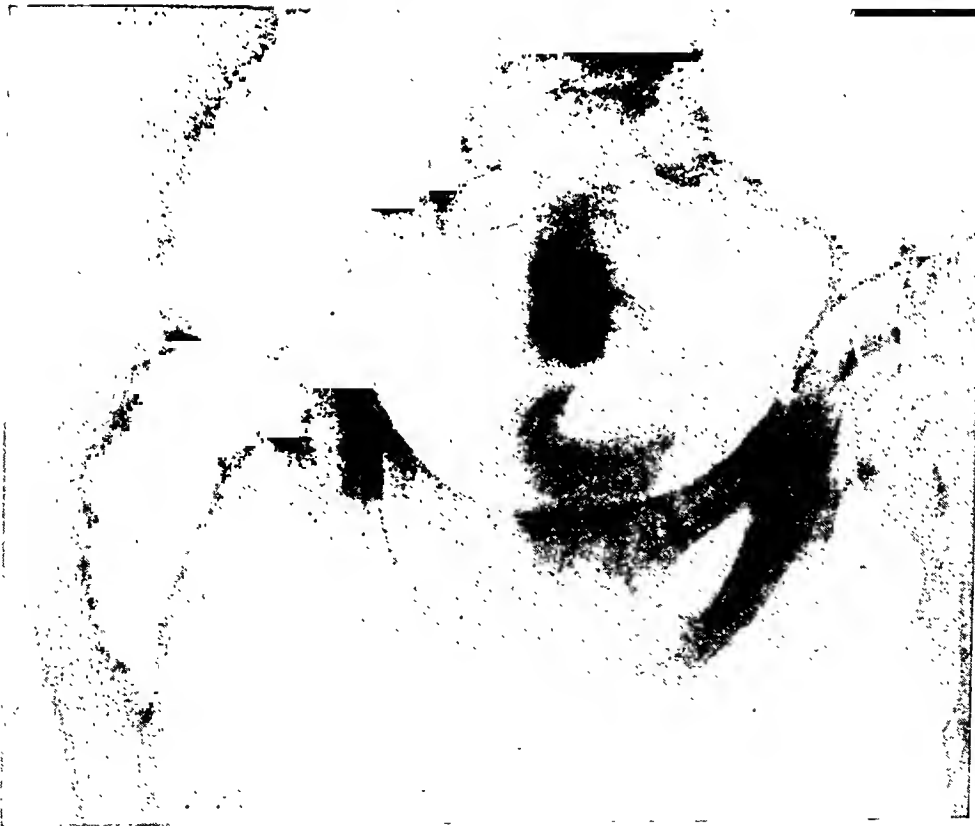


Fig. 6.

are agreed being that they are neither tuberculous, rachitic nor syphilitic. Legg considered trauma to be the sole determining ætiological factor, acting by interfering with the vascular supply of the epiphysis and leading to hyperæmia, which according to Leriche's view causes rarefaction of bone. In support of this theory is the frequency of a history of injury, the more common occurrence of the condition in boys, and its location in weight-bearing joints such as the hip or in epiphyses subjected to strain as in the tubercle of the tibia. At one time the infective theory appeared to be most convincing, as Legg himself grew cultures of *Staphylococcus aureus* from material scooped out from the femoral neck, and Phemister found definite histological evidence of an inflammatory lesion. These observations have not been confirmed, but the balance of evidence is in favour of the condition being due to the action of attenuated organisms circulating in the blood which settle in an epiphysis subjected to mild trauma. Hence the slight rise of temperature, swelling and pain which are often present in the early stages, the irritability of the joint as evidenced by muscular spasm and the fact that the disease is frequently bilateral. Our knowledge of its pathology is derived almost entirely from the study of radiological appearances. In the early stages the epiphysis becomes flattened and thinned out and may show division into several pieces—'fragmentation'. Later the fragments coalesce and recalcification is established. The head becomes flattened and as it expands 'creeps' out of the acetabulum. The upper part of the neck becomes expanded and shortened, and ill-defined areas of decalcification may form in its upper part, to be replaced later by areas of condensation. These changes may persist throughout life and definitely predispose towards osteo-arthritis at a later age. In 51 per cent a permanent limp and restriction of hip movements resulted. These cases are generally received with a diagnosis of early tuberculosis of the hip joint, but the diagnosis from tuberculosis presents no difficulty if one considers the freedom from pain, the good general health of the patient, and that only certain movements are limited. The radiogram settles the diagnosis at once.

This patient was anesthetized and the limb was put up in plaster of Paris in abduction, after correcting the adduction and flexion deformity. Three months later the splint was removed and a caliper walking splint was fitted. One month later the patient was discharged walking well and free from symptoms. The radiogram (figure 5) showed the head of the femur beginning to take on a shape approaching the normal, with less sclerosis.

As a rule one loses sight of hospital cases, but in this instance I am greatly indebted to Dr. Weldon, Chief Medical Officer, A. B. Railway, for sending me a report on the subsequent

progress of the boy and a radiogram (figure 6) taken in January 1933. It shows uniform density of the neck and epiphysis, some flattening and mushrooming of the head and flattening of the top of the neck with slight coxa vara, changes which are the reason for the name 'coxa plana' often given to the end-results of the disease. The caliper splint was worn for 18 months and then discarded as there was no pain or discomfort, movement in all directions was then almost normal and there was only a slight limp. Considering the marked deformities shown in the skiagram the clinical result is far better than one would expect. It is to be hoped that this result will be permanent, but it appears likely that the deformed articular surfaces will become the seat of an osteo-arthritis later, which will lead to permanent impairment of movement.

Case IV.—Arthritis of the hip joint producing changes similar to those of Perthes' disease.

N. B., Bengali Hindu boy, aged 12 years. No history of previous disease. Three months ago he slipped and fell on the right hip whilst playing. He was so severely injured that he was unable to rise and had to be carried home. Pain, fever and swelling of the parts around the hip joint followed and persisted for 8 to 10 days, after which the fever and swelling subsided, but the pain persisted and he has walked with a limp ever since. On examination the right side of the pelvis was found to be raised, the right thigh wasted and lumbar lordosis present. Thomas' test showed the right hip joint to be fixed in 20° of flexion and the limb adducted with gross limitation of abduction, so that only 15° of abduction was possible. The radiogram (figure 7) shows flattening, sclerosis and fragmentation of the femoral epiphysis. Areas of rarefaction are seen in the epiphysis, contiguous portions of the femoral neck and acetabulum. The radiologist reported that the appearances suggested pseudo-coxalgia with added infection.

The treatment was on the same lines as in case III, a plaster-of-Paris splint in abduction for two months and then a caliper splint to be worn for a year or more. On removal of the plaster splint the radiogram showed evidence of re-formation of the head of the femur, the sclerosis largely disappearing and some decalcification of the femoral neck, probably due to disuse. The patient was discharged after six months, walking in the splint without difficulty and with no apparent limitation of movement. He has not been seen since his discharge.

The interest of this case lies in the similarity of the x-ray appearances to those shown in figure 5. There is here a definite history of a traumatic arthritis following injury, with fever, pain, swelling and definite evidence of inflammation. In the previous case there was no such history, but the radiological appearances during the recovery stage are indistinguishable from those in case IV. The conclusion that the disease is of inflammatory origin seems clear from a comparison of these two cases, though the inflammation may be of such a low grade that in many cases it does not give rise to sufficient disability to attract attention. Cases such as this, of which several have come under the writer's notice, throw an interesting light on the ætiology of the disease.

The treatment of unreduced dislocation of the hip

In this country one frequently meets with cases of unreduced dorsal dislocations of the hip joint which have been out for more than three months, sometimes for a year or more. The advice given in the textbooks to reduce them by open operation is not always easy to follow. The operation, involving the complete stripping of all the muscles attached to the upper end of the femur, is a very formidable one and the scooping out of the filled-up acetabulum is no easy matter, even when this has been done it may be impossible to retain the bone in the acetabulum. If the operation is successful the joint is stabilized, but the range of movement is usually very small. In cases of over four months standing the operation is quite likely to fail and the head to slip out again. For such cases there is another procedure, which accomplishes the main object to be aimed at, the stabilization of the hip, without interfering with the joint and is therefore an operation attended with little risk; this is Lorenz's bifurcation sub-trochanteric osteotomy. The femur is divided just below the great trochanter by an oblique osteotomy and the lower fragment is forcibly abducted and pushed up to impinge against the pelvis below the acetabulum, which then takes the body weight. The result is to stabilize the hip and by permitting tilting downwards of the pelvis on the affected side to compensate the real shortening by an apparent lengthening, better called a 'functional' lengthening. The operation is not at all severe and after it is completed the limb is fixed in plaster for six months and then a caliper walking splint is fitted. The upper fragment unites with the side of the lower fragment and the result is a strong union with a slight degree of movement between the lower fragment and the pelvis, giving excellent function compared with the condition of the patient before operation.

Ankylosed hip joints with adduction deformity

Cases in which the hip joint has been allowed to ankylose in extreme adduction—usually a firm fibrous ankylosis—are extremely common, following gonorrhœal or rheumatoid arthritis. It is usually impossible to break down the adhesions in the joint, as there is much decalcification and atrophy of bone, so that fracture of the neck of the femur with the risk of non-union is very likely to occur if the attempt is made. In these cases there may or may not be real shortening, but there is functional shortening due to the adduction, which raises the pelvis on the affected side by as much as two inches. Lorenz's bifurcation osteotomy is by far the best operation for these cases, achieving a better result than the old simple sub-trochanteric osteotomy. By abducting the femur the pelvis will come to be tilted down on the

diseased side when the legs are parallel and thus functional lengthening will be made to counteract real shortening; as much as 2 inches may thus be gained. The axis of the femur comes to lie under the line of weight of the body instead of outside it and there is a wide area of contact between the pelvis and the upper end of the femur, by which the body weight is transmitted. The writer has performed this operation several times with most satisfactory results and has come to prefer it in such cases to the tedious method of gradual forcible breaking down of adhesions with fixation in plaster, involving several anæsthetics and much painful after-treatment. Figures 8 and 9 illustrate well the principles of the operation.

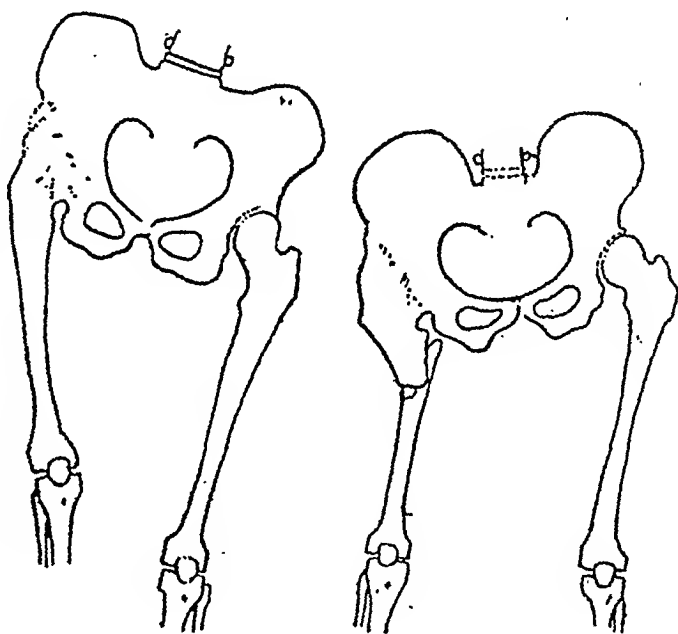


Fig. 8.

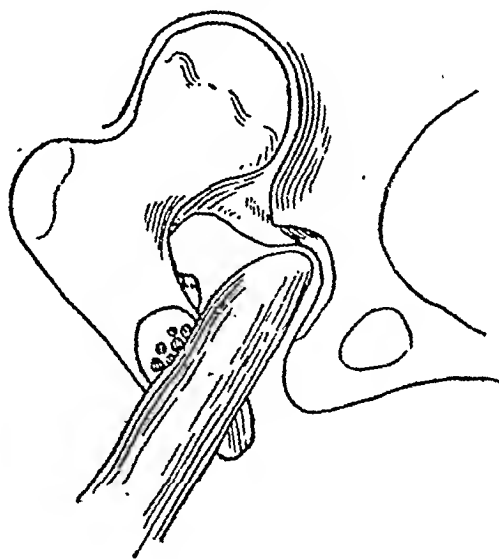


Fig. 9.

My thanks are due to Dr. S. G. Galstaun, Hon. Radiologist to the Medical College Hospital, for the radiograms which illustrate this paper.

CREEPING ERUPTION PRODUCED BY HOOKWORM LARVÆ

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DALGETTY (1901) defined and described 'water-itch' in tea-garden coolies. Bentley (1902) wrote a valuable paper on the subject which it is proposed to abstract on account of its historical interest and because it appears to have been overlooked by most workers during recent years.

The condition of 'water-itch' or 'pani-ghao' is well recognized in tea gardens in Assam, Cachar, and Sylhet, and a similar affection has been noticed in sugar plantations in the West Indies, according to the report of the surgeon-general for Trinidad for 1900. The condition is always associated with the presence of the larvæ of *Ancylostoma duodenale* in the soil. There is a definite seasonal incidence, the disease being common in wet weather and absent in the dry season; all classes of the community may be attacked, but it is not common in Europeans. It attacks individuals with a frequency directly proportional to their exposure to infection and everything points to the earth being its source.

The first symptom is itching and burning, and within one to twenty-four hours a slight papular eruption occurs though at times only a slight erythema is visible. If treated early this eruption may be aborted in two or three days, but if allowed to run its course vesicles which form are liable to burst and to give rise to ulcers, or they may become pustular and unless speedily opened the secondary infection may spread and burrow under the surrounding skin so that extensive ulceration and sloughing may take place.

Scheult and Trinidad considers the disease is caused by a chemical irritant in the soil, and Dalgetty considers it allied to scabies and caused by a similar parasite. The following experiments were made to test the above theories:—(1) A small amount of soil known to be infected was collected and divided into two parts and one part was applied to the arm for about six hours where it produced a typical water-itch. Both the soil from the arm and the unused portion were then examined and no mites were found in either sample, but among other organisms present hookworm larvæ were identified in the unused sample, but they were not found in the portion that had been on the arm. (2) A portion of the same earth was 'sterilized by being baked', and when moistened and placed on the arm no reaction was seen, thus disposing of the chemical irritant theory.

Numerous cases of water-sore were investigated; blood films taken from infected areas, when only in the erythema stage, showed nothing abnormal, but in surface scrapings from similar spots on the skin, discarded sheaths of hookworm larvæ were recognized.

To prove the source of infection, soil was sterilized by heat and after moistening it was inoculated with faeces containing hookworm eggs, and a control culture was made with faeces in which hookworm eggs were not found. After incubation at air temperature for a week the first culture was found to contain many hookworm larvæ and in the second one none were found. These cultures were each divided into two parts, and one part of each was dried, the others being left moist. All four samples were now applied to arms of volunteers and left for about eight hours. The site of application of the untreated portion of the positive culture exhibited typical water-sore lesions, the other three sites only showed slight transient erythema. Examination of the four soil samples after removal from the skin showed in the first untreated portion only a few dead larvæ, in the treated portion of this culture were many dead larvæ, and the other two from the negative culture were still negative. Examination

of both the dried and undried cultures that had not been placed on the skin showed that the drying had killed the larvæ. The results of these experiments are in accord with the epidemiological fact that water-sore is common in the wet season and absent in the dry weather.

In the light of later information it is probable that Bentley's observations apply to *Necator americanus* as well as to *A. duodenale*, but the former species had not been identified when he wrote his paper, so all his references are to the latter worm.

From Bentley's description of the vesicular stage of the eruption it is clear that he saw the type of lesions now known as creeping eruption, but probably owing to the fact that his cases all had multiple infections the intertwining of the individual tracks masked their linear nature.

In the description by Looss (1911) of infections on his own skin with hookworm and strongyloides larvæ, he says that he produced lesions of a linear character similar to those proved by Russian workers to be due to fly larvæ. He first noted this in 1898, so this is apparently the first record of the association of creeping eruption with hookworm larvæ which the following quotation makes clear. 'Personally I have not the least doubt that in my case only a migrating *Agchylostoma* or *Strongyloides* larva can have been the cause of the phenomenon; in the attacks before 1904 only *Agchylostoma* larvæ'.

But the first association of creeping eruption with a nematode is that of Levinsen (1889), who identified a worm taken from a Siamese woman as *Cheiracanthus siamense*, which was later renamed *Gnathostoma siamense* by Leiper (1909). These records of Looss and Levinsen should be clearly distinguished from that of Lee (1874) who first used the name creeping eruption without finding the cause; it was probably a fly larvæ in his case, however, because it occurred in England. A great many of the earlier records of creeping eruption give no cause at all or assume it was due to fly larvæ. Many of these references are American, and on account of the uncertainty of the etiological factor it is not considered worth while discussing these papers in detail, therefore the reader is referred to a paper by Klauder and Greenbaum (1921) who give a long list of references. Many of these papers are of interest because those cases which are reported from the Southern States, or mention a definite association between contact with sand and the appearance of the eruption, are almost certainly due to hookworm larvæ. Although the records of hookworm creeping eruption probably begin with the publication of a paper by van Harlingen (1902) the first really important contribution to the subject was a paper by Kirby-Smith (1915) in which he describes thirty cases seen by him in Florida; he differentiates it from uncinariar dermatitis or 'ground itch' which is

common in this area. Even now that the etiological factor is clearly proved certain workers maintain this distinction.

Parham (1916) reported one case and recorded seeing another in South Carolina both of which were probably hookworm infections in view of the region in which they occurred. Fülleborn and da Rocha-Lima (1919) discuss creeping eruption with special reference to West Africa; they lay greatest stress on *Gastrophilus* larvæ as the causative parasites, but they refer to Looss' record of its production by *ancylostoma* and *strongyloides* larvæ. There is an account of a single case by Ketron (1921) which is of interest because although the cause is not given it is apparently the first record of a cure by the use of a freezing agent.

Kirby-Smith (1925) gave another useful contribution describing the clinical and epidemiological manifestation of this disease, in Florida particularly; in this paper he records his experience of fourteen years in which he saw 2,500 cases. Although the actual cause was still undiscovered a special analysis of 300 of these cases showed that 95 per cent of them had a history of contact with damp sand. In a further study of the disease Kirby-Smith, Dove and White (1926) report the finding of nematode larvæ in five out of forty-eight portions of excised skin. The larva was reconstructed from serial sections and given the name *Agamone-matodum migrans*, and Dr. B. H. Ransom to whom the material was referred stated that it was a third stage larva of a species in the superfamily *Strongyloides*. The context shows that this is obviously a misprint for *Strongyloidea*. It is also of interest that in this paper they trace some connection between soil contaminated with human faeces and creeping eruption. Shinn (1927) reported a single case in which the parasite was not found but in which there was a history of contact with damp sand. Cultures of the faeces of dogs and cats infected with *A. braziliense* and *A. caninum* were made by White and Dove (1927) and applied to their own skins; they produced typical lesions of creeping eruption.

Hamilton (1927) in Australia recorded a case of a child, accustomed to go barefoot, with creeping eruption on both feet. No parasite was found; but in the light of the work of Heydon (1929) this was probably a case of hookworm creeping eruption. From a series of experiments White and Dove (1928) came to the conclusion that the larvæ of *A. braziliense* caused creeping eruption, but those of *A. caninum* failed to do so. Shelmire (1928) records the results of the infection of eighteen individuals each with about one hundred larvæ of *A. braziliense*; sixteen developed typical lesions, and there was no evidence of intestinal infection afterwards. He also states that creeping eruption and ground itch are quite different. Cawston (1928) reported a similar skin disease in South Africa locally known as 'sand-worm

disease' which is probably hookworm creeping eruption. Eight cases of creeping eruption from Lagos, West Africa, were described by Smith and Elmes (1928), but the causal parasite was not mentioned. A useful clinical account is given by Smith, Dove and White (1929) but it adds no new facts. Heydon (1929) records creeping eruption as common in Townsville, Australia, where both cats and dogs are heavily infected with *A. braziliense* and *A. caninum*. He produced artificial creeping eruption with the larvæ of both species, but failed to find evidence of intestinal infection in any of his cases. He also notes that the length of the tracks varies in different experiments on the same individuals. Larvæ of *Uncinaria stenocephala* were used by Fülleborn (1927) to produce creeping eruption in man. In a further communication on experimentally-produced creeping eruption, White and Dove (1929) reach the conclusion that *A. caninum* larvæ typically produce papules without linear lesions, and that *A. braziliense* larvæ produce the linear eruption, but to what extent the latter produce papules and to what extent the former produce lines as well as papules is not established. A long paper by Hume (1930) is only an account of the condition with no new facts and it contains a long list of references most of which are not cited in the text. Le Sueur and Hutchison (1930) give an account of two cases from Sarawak, Borneo, one of which they state was caused by *A. caninum*, but the evidence for this is somewhat inadequate. Apart from this, however, this report is of value because it is a record of severe natural infections in the eastern hemisphere, and also because it gives an account of the successful treatment of a long-standing case with oil of chenopodium. Another long paper by Dove (1932) is mainly a résumé of the work of himself and his co-workers, Smith and White, but a considerable amount of fresh experimental work is included which will be discussed below in relation to the writer's findings.

Present investigation

In all the experiments recorded below the larvæ were grown on earth previously heated to kill all natural nematode infections. The eggs used in these cultures were obtained from dissected worms which were identified before dissection, or in the case of animals intestinal contents were sometimes used, but only after it had been ascertained post mortem that only one species of hookworm was present in the gut. The larvæ were allowed to grow at room temperature for nine to twelve days, then extracted by Baermann's method overnight, and placed on the skin next morning. The method of inoculation was to place the stated number of larvæ on the skin in water by means of a pipette, and then to sprinkle on sufficient finely-divided helminthologically-sterile soil to take up the

water and prevent it running off. This was covered with a bandage and left for about an hour, when the soil was washed off.

In each group of experiments larvæ from a single culture were employed.

Group I. Twenty larvæ of a nine-day-old culture were placed on the flexor surface of the forearm of each individual.

Nos. 1 and 2. Hindu—Bengali—hospital patients suffering from asthma. No intestinal helminths present. No reaction. No eggs in stools up to thirty days after inoculation.

No. 3. Hindu—Bengali—medical man engaged on laboratory work. No intestinal helminths present. No reaction. No eggs in stool up to sixty days after inoculation.

No. 4. European—medical man engaged on laboratory work. No reaction. Stool not examined.

No. 5. Punjabi—medical man engaged on laboratory work. No intestinal helminths present. Stool negative one month after inoculation.

25th May, 1932. Itching felt three to four hours after inoculation. Nothing visible.

26th May, 1932. Three small papules present.

27th May, 1932. Four papules. Slight itching.

28th May, 1932. Papules unchanged. Two lines about two centimetres in length leading from two of the papules.

29th May, 1932. No change.

30th May, 1932. Lines gone and a fresh papule about three centimetres above the original group.

4th June, 1932. All signs gone except slight redness.

No. 6. European—medical man engaged on laboratory work. Slight mixed infection with *A. duodenale* and *N. americanus*.

25th May, 1932. Slight itching in less than half an hour after application of larvæ. On removal of bandage in one hour a small papule surrounded by an area of erythema about two centimetres in diameter was noted. Three hours later the redness had gone and a second papule was present.

26th May, 1932. Vesicles on summit of papules. Slight itching.

27th May, 1932. Vesicles coalesced and growing bigger, surrounded by erythema. Area of œdema about seven centimetres in diameter surrounded by erythema with vesicle in centre. Itching slight and intermittent. No pain or tenderness.

28th May, 1932. Vesicles somewhat enlarged with a palpable line about two centimetres long leading from the central lesions. Œdema unchanged.

29th May, 1932. Vesicles unchanged. Line gone. Œdema lessened. Itching stopped.

30th May, 1932. Vesicles unchanged. Œdema gone. Vesicles opened and dressed with dry boracic acid powder.

The lesion gradually healed and disappeared without further signs or symptoms.

Group II. Thirty larvæ from an eleven-day-old culture of *A. braziliense* from a cat were placed on the flexor surface of the forearm of each individual.

The first six cases in this group were all hospital patients and natives of Bengal.

No. 7. Hindu, male, aged 8 years. Disease, kala-azar. Ascaris and trichuris infection present.

15th June, 1932. Itching within three hours of inoculation. No signs.

16th June, 1932. One small papule. No itching.

17th June, 1932. Two papules very close together. Slight œdema. Burning sensation.

18th June, 1932. Vesicles formed over papules and coalesced. Œdema less.

27th June, 1932. Gradual subsidence from third day. All signs gone. No hookworm eggs in stool up to six weeks after inoculation.

No. 8. Hindu, male, aged 25 years. Disease, kala-azar. Hookworm eggs in stool before inoculation.

15th June, 1932. Itching within three hours of inoculation. No signs.

16th June, 1932. One papule. Slight itching.

17th June, 1932. Three papules. Itching with signs of scratching. Gradual subsidence with nothing further of note except recurrence of itching without any signs, one week after inoculation. Stool not examined.

No. 9. Indian Christian, male, aged 50 years. Occupation, laboratory attendant. Stool negative prior to inoculation. No reaction until twelve days later when a patch of œdema about five centimetres in diameter appeared at the site of inoculation. There was slight tenderness and the man said he could feel something moving. No further signs developed and all were gone one week after their onset. The stool was negative up to thirty-seven days after inoculation.

No. 10. Hindu, male, aged 20 years. Occupation, nil. Disease, hookworm infection. Itching on day of inoculation, with no signs. Nothing more noted. Stool not examined.

No. 11. Hindu, male, aged 10 years. Disease, ascariis infection.

15th June, 1932. No reaction.

16th June, 1932. One papule. Occasional itching.

17th June, 1932. Vesicle formed over papule—surrounding small area of erythema. Itching.

18th June, 1932. Two fresh vesicles near original one. Itching increased. No fresh signs or symptoms, and all lesions gone within eight days of inoculation. Stool not examined.

No. 12. Hindu, male, aged 38 years, clerk. Disease, kala-azar. No helminth ova in stools.

15th June, 1932. No reaction.

16th June, 1932. Several deep papules, can be felt but not seen—itching.

17th June, 1932. Small papules visible.

21st June, 1932. All signs gone. The stool was negative until thirty-six days after inoculation when three or four hookworm eggs were found by Lane's centrifuge. These eggs were unusually small measuring only 0.053 mm. in length. The patient was treated the following morning with carbon tetrachloride and oil of chenopodium, and on the following day a single female *Ancylostoma braziliense* was recovered.

No. 13. European. The same individual as no. 4, group I. No reaction. The same person was submitted to a third inoculation with twelve larvæ from a twelve-day-old culture without any result. Stool never examined.

No. 14. Punjabi. The same individual as no. 5, group I. Stool negative.

15th June, 1932. Inoculated on both forearms. The inoculation on the left side was at the same spot as the first inoculation. Three hours after inoculation there was no reaction on the left arm, but slight itching on the right arm.

16th June, 1932. Left arm—one papule. Right arm—two papules.

17th June, 1932. Left arm—two papules. Right arm—no change.

18th June, 1932. Left arm—vesicles. Right arm—vesicles.

Vesicles dried up and all signs gone by 23rd June, 1932.

18th July, 1932. Hookworm eggs in stool by Lane's centrifuge. Eggs small, similar to those in no. 12.

24th July, 1932. Treated with CC14 and oil of chenopodium. No worms recovered.

No. 15. Hindu, medical man. Occupation, laboratory worker. Stool negative before inoculation.

15th June, 1932. Slight itching within three hours of inoculation. No signs.

16th June, 1932. Five discrete papules close together.

17th June, 1932. Six papules—all slightly larger—no itching.

18th June, 1932. Vesicle formation with tendency to coalesce.

20th June, 1932. One fresh papule about five centimetres to right of original group—itching again felt.

21st June, 1932. All but last-formed papule disappearing.

25th June, 1932. All papules again swollen and itching with a fresh one to the left of the original group.

27th June, 1932. Slight increase in size—itching still troublesome.

30th June, 1932. All signs nearly gone.

18th July, 1932. A few small hookworm eggs in stool.

22nd July, 1932. Treated with CC14 and *ol. chenopodium* and two female *Ancylostoma braziliense* obtained from the stool on the same day.

No. 16. Hindu, medical man. Occupation, laboratory worker. Stool negative.

15th June, 1932. Slight itching within three hours of inoculation. No signs.

16th June, 1932. No signs or symptoms.

17th June, 1932. Two reddish macules—no itching.

18th June, 1932. Macules gone—one small papule appeared.

20th June, 1932. Papule increased and two fresh ones present—itching marked.

21st June, 1932. No change—itching less.

24th June, 1932. Subsiding.

21st July, 1932. A few small hookworm ova in stool. In this case immediate treatment was not possible and when the stool was examined on 1st August, 1932, it was negative, and remained so on three or four subsequent examinations. This was apparently a transient infection.

No. 17. Mahomedan. Occupation, laboratory attendant. Hookworm and ascaris infection.

15th June, 1932. Slight itching within three hours of inoculation. No signs.

16th June, 1932. A single large papule with vesiculation.

17th June, 1932. Began to subside and no signs one week after inoculation.

21st July, 1932. Treated with CC14 and *ol. chenopodium* and two female *Necator americanus* recovered.

22nd July, 1932. Four male and two female *N. americanus* and one male ascaris recovered.

Not included in group II.

No. 18. European, medical man, the same individual as no. 6, group I.

27th June, 1932. Inoculated with ten larvæ of *A. braziliense* from a different culture, on the flexor surface of the left forearm. No reaction. Two other larvæ from the same culture were placed on the flexor surface of the left wrist and itching was felt about four hours afterwards with the formation of a small wheal.

28th June, 1932. Wheal replaced by a large red macule, in the centre of which a group of small vesicles are visible with a hand lens.

29th June, 1932. Track formation beginning with intermittent itching. This continued at intervals until 2nd July, 1932, from which time the lesion began to subside without treatment. The total length of the track was not more than six centimetres.

Group III. Thinking the comparative lack of reaction in all the above cases might be due to unusual thickness of the skin a series of four Indian hospital patients were taken and were all inoculated on three different parts of the body where the thickness of the skin is of marked difference. The spots where each one of the four persons was inoculated were the extensor and flexor surfaces of the forearm, and the web between the great toe and the second toe of the foot. Fifteen larvæ were placed on each spot and there was no reaction in any of the cases. These experiments were carried out in November, and although it was somewhat cooler than when the earlier experiments were done the difference in temperature was not considered sufficient to have any effect on the result.

Ancylostoma caninum.—Eleven individuals were utilized in experiments with larvæ from this species of hookworm, and twenty-six inoculations were performed altogether. The method of preparing larval cultures and of inoculating them was exactly the same as in the case of *A. braziliense*, so it needs no detailed

description. About thirty larvæ were placed on the skin on each occasion. Most of the results were entirely negative, but in a few of them small papules or tracks, never more than three centimetres in length, were noted; in the cases showing these signs there was a slight amount of itching. All signs of larval activity in the skin disappeared in a few days in all instances, and in none of the cases in which stool examinations were frequently made was any evidence of intestinal infection found. The people used in this series were with one exception, who was an Anglo-Indian, all Indian inhabitants of Bengal similar to those mentioned in the *A. braziliense* groups.

One other person, the same European as no. 6, group I, was twice inoculated with *A. caninum* larvæ.

On the first occasion four larvæ were placed on the radial side of the left forearm a little above the wrist, and for two days there was no reaction, when a moderately hard deep wheal developed accompanied by some itching. Nothing further was noted and the lesion gradually disappeared. A second inoculation with a single larva was made two inches above the first but three days later. A vesicle surrounded by erythema and slight deep swelling appeared the following day. The condition appeared to be subsiding but three days after the inoculation a large wheal near the original vesicle suddenly appeared and was intensely itchy, by the next morning the wheal had gone and in its place there was a track curved on itself, and of a total length of about four centimetres. No further signs or symptoms occurred and the lesions gradually disappeared.

Ancylostoma duodenale.—Six tea-garden coolies in hospital with Naga sore (tropical ulcer) were utilized in this experiment. Four were Nepalis, and two were Hindus, and all of them had hookworm infection. The larvæ were obtained from cultures of worms removed from human beings post mortem. The site of inoculation was the flexor surface of the right forearm, and only ten larvæ were used on each, because of the pathogenicity of this species.



Eruption on forearm of a Nepalese coolie on the fourth day after inoculation with ten *Necator americanus* larvæ.

Three of the cases had no reaction and the others had papules going on to vesicle formation with short typical tracks leading from them; all signs had vanished within six days of inoculation.

Four more hospital patients were inoculated on another occasion on both the flexor and extensor surfaces of the forearm and only one of them showed any reaction and this was similar to the positive results in the first series. It is interesting to note that the reaction appeared on both front and back of the forearm so

that the thick skin of the back was no more resistant than the thinner skin on the front.

Necator americanus.—The six patients in the first series of *A. duodenale* experiments were inoculated at the same time, on the flexor surface of the left forearm each with ten larvæ of *N. americanus* procured in the same way as those of *A. duodenale*, and they all showed a definite vesiculo-papular eruption of linear type at the site of inoculation. The most extensive lesion was that shown in the illustration, and even this one had practically disappeared in ten days without treatment. Nine other persons, eight Indians and the European, no. 6, group I, were inoculated on different occasions and all gave a positive reaction with definite lines of vesicles, but none were so marked as in the case illustrated above. It is of interest to note that three of these inoculations were done in January of this year while the weather was exceptionally cold, so that a high temperature does not appear to have much influence in producing positive results.

The six coolies treated with *A. duodenale* and *N. americanus* larvæ gave three positive results with the former and six with the latter species, so it was thought that they might be particularly susceptible to this type of infection. They were accordingly all given an inoculation on the forearm with twenty larvæ of *A. caninum* with entirely negative results.

Discussion

It was pointed out by Maplestone (1929) that creeping eruption as seen in the United States of America and elsewhere is apparently absent from India, and the same thing has been noted by Africa (1932) in the Philippine Islands. Africa, however, produced severe creeping eruption in two Filipinos with larvæ of *A. braziliense* grown in the Philippines. He suggests as an explanation of the absence of this condition in nature in these islands that there may be a different race of *A. braziliense* in the East Indies and in America, and that the eastern strain having been fairly often recorded as a human parasite is better adapted to the human host than the American strain which has only once been found in man by Gordon (1922). The result is that the eastern strain passes directly through the skin to the gut, while the American strain not being adapted to the human gut wanders in the skin. His own experiments with the eastern strain appear to upset this theory, which is further discounted by Dove (1932) who mentions making use of a boy in his experiments who was found in Texas naturally infected with *A. braziliense*, and who from the description of the use made of his stools carried this infection for a fairly long period. Another objection to the race theory is that in Australia and probably in Borneo, both countries in the same zoological area as the Philippine Islands, strains of hookworm larvæ exist that are capable of producing severe creeping eruption. In his work Dove (1932) made cross-breeding experiments with strains of *A. braziliense* from different parts of the Southern United States. The adults of these strains showed slight morphological differences, and he showed there was no specific difference, therefore, if different strains of this species do exist, morphology is not likely to be of any more use in differentiating them than

it is in the case of the ascaris of man and the pig. Dove also found that larvæ cultured direct from the stool of the boy with *A. braziliense* infection only produced an abortive eruption whereas after passage through a cat the larvæ from this strain of human origin produced a typical eruption which persisted for at least thirty days. This does not agree with my findings, for all the larvæ of *A. braziliense* used by me, all of which failed to produce more than an abortive eruption when they produced any at all, were cultured direct from worms which came from cats.

At a later stage in his experiments, using material from the same boy, Dove infected previously-worm-free human beings, cats and dogs with larvæ grown from his stools, and, in the subsequent examination of the infected persons and animals, recovered *N. americanus* and *A. caninum*. He assumed that the boy's infection had changed from one of simple *A. braziliense* to a mixed one with *N. americanus* and *A. caninum*. He offers no explanation how this strange alteration of species might have occurred, and in the writer's opinion this statement must be accepted with reserve, especially in the case of *A. caninum*, for as far as can be ascertained there is only one record of this species being found in human beings and that is by Manalang (1925).

Whatever the factors may be, and for these none of the existing theories offer an explanation, it seems clear from the above experiments that severe creeping eruption, if it exists in India at all, must be very rare. As far as my experience goes with different races of host in these experiments, there is no evidence that race has any influence on the amount of skin reaction to hookworm larvæ of any of the four species employed. There is a slight indication of individual sensitiveness however, for no. 6, group I, was carrying a light mixed infection at the time of inoculation, and what is probably more important, has been engaged on helminthological work for many years. The type of reaction produced in this instance had certain allergic signs and it is of interest to note that the description of what was probably *N. americanus* infection in an endemic area given by Smith (1904) could be fairly well applied to the first lesion in this case. That special sensitization to nematode proteins may be produced in man is shown by Fülleborn (1930) who described a very severe reaction involving his whole arm and arising after infection with probably only one *A. caninum* larva. He has sensitized himself by repeated experimental inoculations over many years.

It is held that the larvæ of *A. braziliense* always, and of *A. caninum* occasionally, produce creeping eruption because they are wandering in the skin of an unsuitable host. This theory presupposes an undue amount of prophetic knowledge or instinct in the larvæ, for it is difficult to believe that the larvæ remain in the

skin because they are aware the intestine of the animal in which they happen to be is unsuitable for them in their adult stage. The present series of experiments indicate that this theory is not tenable, for as far as creeping eruption can be produced in India the larvæ of *N. americanus* appear to be the most certain and most active species in causing a skin eruption.

In all the experiments of other workers, quoted above, intestinal infection with *A. braziliense* has never been found in man. After my own experience this is not surprising for by using Lane's centrifuge only three or four eggs were found on a slide and as far as can be judged the infection only lasted a very few days, therefore I am convinced I would have missed the infections I discovered, had I used any other method of stool examination.

With regard to the name 'creeping eruption' it is stated by certain Americans who have written on the subject that this condition and ground itch are quite distinct. Although I have never seen a case of severe creeping eruption I feel convinced, from comparison of my mildest and most severe cases, that the lesion is essentially the same and that the difference is only in degree. Further, the more persistent and extensive a creeping eruption is the more liable it is to secondary infection, which has nothing to do with the primary lesion. These attempts to differentiate different types of creeping eruption will in the end only confuse and complicate the matter in the way that so many of the older skin diseases are already confused.

It has also been suggested that 'creeping eruption' should be specially reserved for this disease in the Southern United States, because it was there that the cause was first proved. Although this argument has some claim to consideration when Lee's original use of the term is considered, it is of no value against Levinsen's case because a gnathostome larva was identified as the cause in this instance in the year 1889. Therefore, if the title to creeping eruption as a name is to depend on the finding of the cause, gnathostome creeping eruption must have it. It may have been noticed that in the present paper the phrase 'hookworm creeping eruption' has been used once or twice. This is not with any idea of creating a name but it was found short and explanatory for the subject under discussion in the context.

Almost all the papers that have hitherto appeared on creeping eruption have given a long history of the condition and have included references to it, whatever has been the cause. This must all be so well known to workers on the subject by now that it has not been repeated here, but an attempt has been made to separate the history of hookworm creeping eruption from the other varieties, and so clarify the subject.

REFERENCES

- Africa, C. M. (1932). Studies on Experimental Creeping Eruption in the Philippines. *Philippine Journ. Sci.*, Vol. XLVIII, p. 89.
- Bentley, C. A. (1902). On the Causal Relationship between 'Ground itch', or 'Pani-ghao', and the presence of the Larvæ of the *Ankylostoma duodenale* in the Soil. *Brit. Med. Journ.*, Vol. I, 1902, p. 190.
- Cawston, F. G. (1928). The Creeping Eruption of Natal, known as Sand-worm Disease. *Journ. Trop. Med. and Hyg.*, Vol. XXXI, p. 201.
- Dalgetty, A. B. (1901). Water-itch or Sore Feet of Coolies. *Journ. Trop. Med. and Hyg.*, Vol. III, p. 73.
- Dove, W. E. (1932). Further Studies on *Ancylostoma braziliense* and the Etiology of Creeping Eruption. *Amer. Journ. Hyg.*, Vol. XV, p. 664.
- *Fülleborn, F. (1927). Durch Hakenwurmlarven des Hundes (*Uncinaria stenocephala*) beim Menschen erzeugte 'creeping eruption'. *Abhandl. a. d. Gebiet. d. Auslandskunde Hamburg. Univ.*, Vol. XXVI, p. 121. (Festschrift Nocht.)
- *Fülleborn, F. (1930). Ueber die durch die Larve von *Ancylostoma caninum* verursachten Hauterscheinungen (Review *Trop. Dis. Bull.*, Vol. XXIX, p. 425).
- Fülleborn, F., and da Rocha-Lima, H. (1919). Ueber Larbisch und Wolossjakik (Hautmaulwurf). *Arch. Schiffs- u. Trop.-Hyg.*, Vol. XXIII, p. 259.
- Hamilton, G. R. (1927). Larva Migrans in Australia. *Med. Journ. Australia*, Vol. II, p. 875.
- Heydon, G. M. (1929). Creeping Eruption or Larva Migrans in North Queensland and Note on the Worm *Gnathostoma spinigerum* (Owen). *Med. Journ. Australia*, Vol. I, p. 583.
- Hume, E. E. (1930). Wet Sand Creeping Eruption in the Largest American Army Station. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXIV, p. 313.
- *Kirby-Smith, J. L. (1925). A Consideration of Creeping Eruption in the Southern States with an Entomological Report. *Southern Med. Journ.*, Vol. XVIII, p. 402.
- Kirby-Smith, J. L., Dove, W. E., and White, G. F. (1926). Creeping Eruption. *Arch. Dermat. and Syph.*, Vol. XIII, p. 137.
- Klauder, J. V., and Greenbaum, S. S. (1921). Creeping Eruption (larva migrans). *Arch. Dermat. and Syph.*, Vol. III, p. 377.
- Leiper, R. T. (1909). The Structure and Relationships of *Gnathostoma siamense* (Levinson). *Parasitology*, Vol. II, p. 77.
- *Lee, R. J. (1874). Case of Creeping Eruption. *Trans. Clin. Soc. London*, Vol. VIII, p. 44.
- Le Sueur, E., and Hutchison, W. (1930). A Note on the Treatment of Creeping Eruption with External Application of Oil of Chenopodium. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXIV, p. 327.
- *Levinson, G. R. M. (1889). Om en ny Rundorm hos mennesket *Cheiracanthus siamense* n. sp. *Vidensk. meddel. fra naturh. Foren. i Kjøbenhavn f.*, p. 323.
- Looss, A. (1911). The Anatomy and Life History of *Agchylostoma duodenale* Dub. Part II. Development in the Free State. Cairo: National Printing Department.
- Manalang, C. (1925). Studies on Ankylostomiasis in the Philippines. *Trans. Sixth Congress, Far Eastern Assoc. Trop. Med.*, Vol. I, p. 351.
- Maplestone, P. A. (1929). A Case of Human Infection with a Gnathostome in India. *Indian Med. Gaz.*, Vol. LXIV, p. 610.
- Parham, J. C. (1916). Creeping Eruption. Report of a Case. *U. S. Nav. Med. Bull.*, Vol. X, p. 103.
- Shelmire, B. (1928). Experimental Creeping Eruption from a Cat and Dog Hookworm (*A. braziliense*). *Journ. Amer. Med. Assoc.*, Vol. XCI, p. 938.
- *Shinn, H. L. (1927). Creeping Eruption, Report of a Case. *U. S. Nav. Med. Bull.*, Vol. XXV, p. 632.
- Smith, C. A. (1904). Uncinariasis in the South with Special Reference to Mode of Infection. *Journ. Amer. Med. Assoc.*, Vol. XLIII, p. 592.

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THE ARNETH COUNT, WITH PARTICULAR REFERENCE TO ITS DIAGNOSTIC VALUE IN ASTHMA

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The Arneth count.—The neutrophilic polymorphonuclear cell develops from a mononuclear cell with a single round nucleus. The myelocyte passes through an intermediate stage with a single indented nucleus (metamyelocyte), but with no true nuclear lobulation. It is evident, therefore, that the cell with a simple round nucleus is younger than that with an indented nucleus and this form is younger than the true polymorphonuclear cell. Arneth (1904) argued from this line of thought by contending that a polymorphonuclear cell with only one lobe was younger than one with two lobes and so on. He studied blood smears from many different cases of acute and chronic infections and stated that very important morphological changes were found in the nuclei of polymorphonuclear neutrophilic leucocytes. He divided these cells into five classes, the division being based on the shape of the nuclear material:—

Class I containing cells with one round or indented nucleus.

Class II containing cells with two nuclear divisions.

Class III containing cells with three nuclear divisions.

Class IV containing cells with four nuclear divisions.

Class V containing cells with five or more nuclear divisions.

Each class has subdivisions according to the shape of the nuclear portion, whether round or s-shaped, making twenty-five types in all. Arneth counted one hundred polymorphonuclear cells and arranged them in his five classes like this:

I	II	III	IV	V
5	35	41	17	2

This expression is known as the Arneth count.

Arneth stated that the percentage of cells in the various classes varied only within normal

limits in health, but changed in infectious conditions, the change usually being in the direction of an increase in the percentage of classes I and II and a decrease in classes III, IV and V; this he spoke of technically as a 'shift to the left'. Particular emphasis was laid on the prognostic value of this classification in pulmonary tuberculosis. Arneth's classification did not define when a nucleus might be considered as divided and so allowed the personal factor to assert itself unduly. To rectify this Cooke (1914) has given a criterion of nuclear lobulation—'If there is any band of nuclear tissue except a chromatin filament connecting the different parts of a nucleus, the nucleus cannot for the purpose of the Arneth count be said to be divided'; when the count is made according to Cooke's method the average normal figures vary considerably from those obtained with Arneth's method. Cooke (1914 and 1928) gives the following figures as the average normal:

I	II	III	IV	V
10	25	47	16	2

Schilling (1920) simplified Arneth's classification by dividing the neutrophilic cells into the following four groups.

Group I myelocytes.

Group II young metamyelocytes (with only the slightest indentation) of the nucleus.

Group III older metamyelocytes (with deep indentation but no true lobulation of the nucleus).

Group IV polymorphonuclears.

In doing the ordinary differential count of leucocytes, each of these types is counted separately, so that in the result each variety of neutrophilic granular cells is expressed as a percentage of the total number of leucocytes; in Arneth's method they are expressed only as a percentage of the total neutrophilic cells. As a normal figure Schilling gives neutrophilic granular cells 67 per cent—these are composed of 63 per cent polymorphonuclear and 4 per cent of old metamyelocytes (band forms). The young metamyelocytes and myelocytes are absent from the normal blood.

Pons and Krumbhaar (1924) have proposed a further simplification in the Arneth count. They believe that essential clinical purpose is served if all neutrophils are subdivided into three groups as under

- (1) Metamyelocytes (very young) with round or slightly indented nuclei.
- (2) Non-segmented forms (young) where the nuclear material is connected with broad bands.
- (3) Segmented forms (older) where two or more groups of nuclear material are connected by narrow strands of filaments.

Roberts (1927) has recently proposed a still further simplification of the Arneth's classification in which the polymorphonuclear neutrophils are divided into only two groups 'lobulated' and 'non-lobulated'. Roberts states the number of non-lobular forms to be 25 per cent. A non-lobular count of 35 per cent or over (except during menstruation when a normal count may rise up to 35 per cent) is indicative of an acute inflammatory process.

The Arneth index.—In Arneth's count the result is expressed in five sets of figures which is rather cumbersome and it was desirable to replace such an expression by a single figure. Many ways of doing this have been suggested.

(1) Arneth took the sum of the cells in the first two groups as the index.

(2) Bushnell and Treuholtz (1908) proposed the sum of the cells in group I and group II and one half of

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Smith, E. C., and Elmes, B. G. T. (1928). Creeping Eruption in Lagos. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXII, p. 289.

* van Harlingen, A. (1902). Report of Three Cases of Creeping Larva in the Human Skin (Hyponomoderma, Kaposi). *Amer. Journ. Sci.*, Vol. CXXIV, p. 436.

White, G. F., and Dove, W. E. (1928). The Causation of Creeping Eruption. *Journ. Amer. Med. Assoc.*, Vol. XC, p. 1701.

* Original papers not available.

the cells of group III. This index is commonly used as the Arneth index.

(3) Ponder and Flinn (1926) suggested the following:

The cells of each group are multiplied by the number of the group (group I by 1, group II by 2, and so on), the results added, and the total divided by the number of cells counted. The average normal index thus computed is 2.7.

(4) Hamilton-Black's (1913) index is obtained by multiplying the number of cells in class I by 10, the number of cells in class II by 18, the number in class III by 22, and the number in class IV by 25, 100 cells being dealt with altogether. Normally it is about 2,000 and cannot be less than 1,000. It is based on a finding that the phagocytic activity of the cells of various classes are as 10 : 18 : 22 : 25. The use of this index implies the acceptance of these figures for phagocytic ratios, but Ponder and Flinn (1926) were unable to find any significant difference between the phagocytic activity of the various Arneth classes of the polymorphonuclear cells. Ponder (1928) concluded that, so far as diapedesis and phagocytosis *in vitro* were concerned, the cells of various Arneth classes were indistinguishable, for the increase in the nuclear lobulation which occurred with the increasing age of the cell did not apparently enable the cell to pass more readily from the vessels and lymph spaces into infective cavities, nor did it render more active as a phagocyte.

The experimental confirmation of Arneth's theory regarding the age of the polymorphonuclear leucocyte and conformation of the nucleus.—Colbert (1924) using vital stains confirmed Arneth's view of the significant relation between the shape of the nucleus and the age of the cell. In the films he identified several neutrophils with unsegmented nuclei and repeatedly traced the outline of an individual nucleus for three hours. In no instance did any nucleus, once identified as an unsegmented type, become segmented under observation. He is of the opinion that the constant shape of the neutrophile nucleus in the living state for several hours supports the view that the shape of the nucleus was not an accident but bore a definite relation to life history of the cells.

The study of the effect on the Arneth count of substances which stimulate the bone marrow to rapid and increased production of leucocytes provides evidence in favour of Arneth's assumption that the cell with a one-lobed nucleus is younger than that with two, and so on. Lim, Sarkar and Brown (1922) had shown that thyroid substance definitely stimulated the bone marrow in rabbits and this substance has been used by Ponder and Charipper to study the effect on the Arneth count when bone marrow was stimulated. Ponder (1924 and 1926) found that in rabbits repeated injections of thyroid resulted in markedly increasing the percentage number of polymorphonuclears with a simple (immature) nucleus which he thought was due to thyroid stimulating the bone marrow, resulting in the increased production of an immature type of cell. A single injection of thyroid produced a deflection of the Arneth count, a large number of cells of class I being introduced into the circulation; subsequent changes in the count were followed and it was shown that the cells of class I developed in the blood stream into cells of class II, these into cells of class III and so on until class V was reached. Charipper (1929) showed the same effect of thyroid on the Arneth count of a perennibranchiate amphibian.

Another substance definitely known to effect the bone marrow is benzol. Weiskotten and others (1915, 1919 and 1924) have shown that subcutaneous injections in rabbits of an olive-oil and benzol mixture first caused a rapid decrease of leucocytes in the peripheral circulation after which a primary rise occurs, this is followed by a secondary fall and a secondary rise. They noted that the phenomenon was accompanied by a marked aplasia of the bone marrow following the injection with active regeneration occurring at the time of secondary rise. Hunt and Weiskotten (1930) thought that

experimental verification of the interpretation of Arneth's classification would be possible in the conditions brought about by benzol injection. A marked leucopenia was followed by a large number of polymorphonuclear leucocytes being produced rapidly and passed into circulating blood, so that leucocytes known to be in varying stages of life cycles could be studied. From his study he concluded that cells with single-lobed nuclei were young or immature forms, and that the number of lobes increased with the maturity of the cells. According to Cooke the length of life of a polymorphonuclear cell in circulation is about three weeks.

The steady state of the Arneth count.—The constancy of Arneth count in normal and pathological conditions is very remarkable. Ponder (1926) maintains that this constancy was the result of a balance between at least three factors—the production of the polymorphonuclear cells, their removal, and their development from class to class. He came to the conclusion that the distribution among the various Arneth classes was due to the cells remaining a short time in class I, a longer time in class II, a still longer time in class III and so on, the cells normally entering the circulation as cells of class I and leaving it from classes IV and V. The steady state in abnormal conditions, he thought, was due to the cells leaving the circulation from classes earlier than classes IV and V.

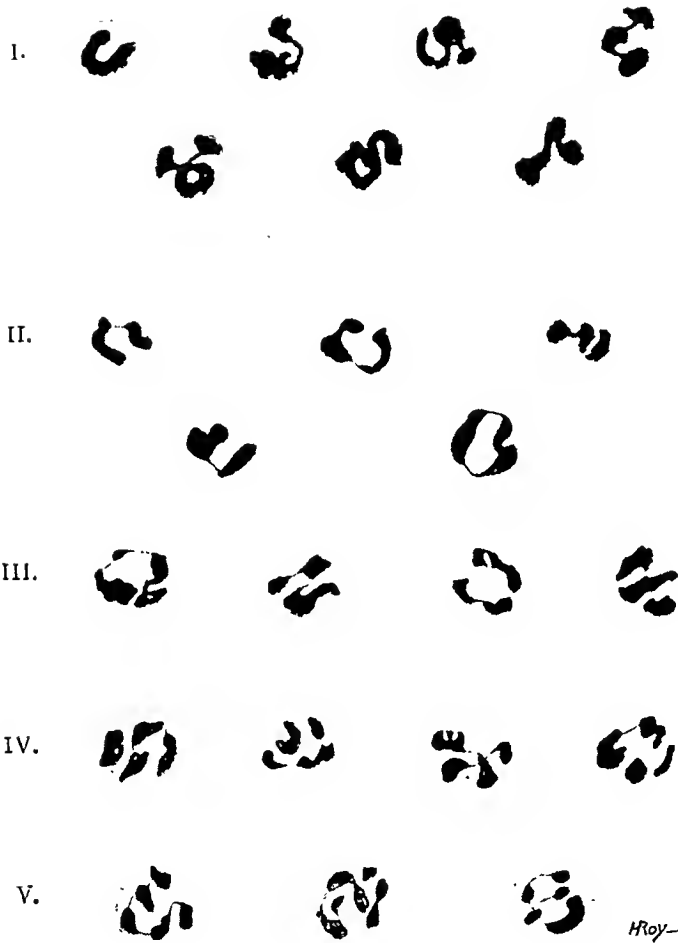
Influence of various drugs, organic and inorganic extracts, colloidal metals, ultra-violet and x-ray exposures on the Arneth count in experimental animals.

A shift to the left with thyroid and benzol has already been referred to. Ponder and Flint (1926) found that the removal of the thyroid in adult rabbits did not influence the Arneth count. They have shown that gelatin, trypsin, colchicin, nucleic acid, ether and thyroxin all deflected the Arneth count in the rabbit to the left and that pilocarpine had no effect. Each one of these substances deflecting the count produced at the same time a polymorphonuclear leucocytosis and they concluded that the substances deflected the count by stimulating the bone marrow and thus causing an outpouring of the younger forms of the polymorphonuclears, which have simple nuclear configuration.

Kennedy and Grover (1928) found that by a single exposure to x-rays the Arneth count in rabbits was deflected to the left. Kennedy and Thompson (1928 and 1929) found a similar shift to the left by an exposure to ultra-violet rays and by injections of various gonad extracts and of pituitrin, adrenalin and insulin. Danzer (1930) found that extracts of various organs and tissues when injected into rabbits deflected the Arneth count to the left, the deflection being due to the contained protein. The destruction and absorption of tissues *in vivo* was followed by a similar deflection. He thought that the deflection in the Arneth count after injury to various tissues might possibly be explained by that observation. He further suggested that the continual and normal break-down of tissue in the body was sufficient to provide a stimulus for the continual and normal output of polymorphonuclears by the bone marrow. Climenko (1930 and 1932) found that administration of irradiated ergosterol deviated the Arneth count to the left in the same way as an exposure to ultra-violet rays. He found that small doses of colloidal preparations of iron, cobalt, tin, copper, strontium, and nickel produced no significant deflection in the Arneth count. When these substances were given in doses from two to eight times greater than the minimum dose they produce a marked left-handed shift. Intramuscular injections of colloidal calcium and intravenous injections of calcium chloride also caused the count to be deflected to the left. He suggested that the effect of these substances was a non-specific one, due to a deviation in the normal concentrations of the inorganic constituents of the blood serum.

Clinical significance of the Arneth count.—The narrow limits within which the count varies in health has been alluded to. Most pathologic conditions which produce any change cause a shift to the left, that is, a

PLATE VII



Some of the nuclear formations met with in the cells
in various Arneith classes

high index. Cooke (1928) states that in all cases of microbic infection there is an increase in the percentage of the younger cells of classes 1 and 2, and a diminution in classes 3, 4 and 5. According to Cooke an increase in the cells of classes 1 and 2 above 40 indicates toxæmia.

That the Arneth count is deflected to the left in various forms of tuberculosis in man is well known. Ponder and Flint (1928) found that in experimental tuberculosis in the rabbit there was a left-handed deflection of the Arneth count, as in the disease in man. The deflection to the left is so constant in tuberculosis that some observers have come to the conclusion that the appearance of the deflection is diagnostic of the disease. Arneth—for example believed that this left-handed deflection occurred only in tuberculosis of active nature and in such cases alone, and when it occurred in other infections he thought that those infections were to be regarded as superimposed on a tuberculous basis; but Cooke (1914) showed that this view had no foundation and that the Arneth count could be deflected in a condition which had no tuberculous basis. He emphasized the occurrence of a left-handed shift as a constant occurrence in tuberculosis, but insisted that it was not characteristic of the disease alone. In tuberculosis the Arneth count was thought to be of great prognostic value, the higher the index the worse was the outlook thought to be. Arneth assumed that the cells with 1 and 2 nuclei were less resistant than the cells with 3, 4 and 5 nuclei and that when those less resistant cells were present in large numbers the severity of the case varied directly as the number of these cells. Hamilton-Black (1913) found that the phagocytic value against tubercle bacilli of the cells with 1, 2 and 3 and 4 nuclei was as 10 : 18 : 22 : 25. He observed that in certain cases of tuberculous disease tuberculin treatment improved the Arneth count making the shift to the left less marked. Holroyd (1913) studied the Arneth count in thirty cases of tuberculosis and arrived at the conclusion that in cases with unfavourable aspects the cells with one or with two nuclei were present in greater numbers than normally and that as the improvement in general condition took place the drift to the left of the picture was not so marked. Kennedy and Flint (1930) found that the Arneth count in cases of surgical tuberculosis treated by natural heliotherapy in the Alps did not show so great a left-handed deviation as in similar cases treated in Britain. They suggested that the fact might be taken as one of the indications of success of that method of treatment. This prognostic value of the Arneth count in tuberculosis has been very much disputed. As already mentioned, Ponder and Flint (1926) and Ponder (1928) could not confirm the findings of Hamilton-Black regarding the relation between phagocytosis and formation of the nucleus. They found that increase in nuclear lobulation which took place with increase of the age did not render the cell more active as a phagocyte.

A low index, i.e., a shift to the right occurs in pernicious anæmia. Fleming (1929) quoted a case of pernicious anæmia on treatment with liver extract, which showed an abolition of the marked shift to the right in the count, as the total blood picture returned to normal. When the liver treatment was stopped the polynuclear count moved over to the right and was again restored to normal by the liver treatment.

Egloff (1926) draws the following conclusions from his investigation on a shift to the right in the Arneth count.

(1) A shift to the right is observed in about 20 per cent of healthy persons and is a constant and stable characteristic for certain groups.

(2) In many sick persons a shift to the right is a constant phenomenon which may be indicative of certain diseases or functional conditions, perhaps an expression of diminished ability to react.

(3) This form of shift is apt to be encountered more often in stubborn and chronic processes.

(4) Under solar or serum therapy the tendency is to convert the shift to the right toward a shift to the left in connection with clinical improvement.

(5) In patients normally presenting a shift to the right, an active process is not always accompanied by a shift to the left.

The technique.—For the Arneth count scrupulously clean slides and thin well-stained films are essential. The slides should be put in sulphuric acid overnight and washed well in running water for four hours or longer to remove all traces of the acid. They are next washed in distilled water and then in alcohol and stored in absolute alcohol. At the time of using the slide is thoroughly dried with a piece of clean linen.

Leishman's and Jenner's stains are not satisfactory for the nuclei are poorly stained and the granules of the cytoplasm are too prominent. Giemsa or Wright's stains are quite satisfactory, but the stain which is strongly recommended and which we have found very satisfactory is hæmatoxylin and eosin—this stains the nuclear structure very clearly whilst the neutrophilic granules are not stained. The smear is fixed in methyl alcohol and stained with Delafield's hæmatoxylin solution for 3 to 5 minutes. The slide is washed well in water and as a counter-stain a 0.5 per cent solution of eosin is applied for a minute or so. The slide is again washed, dried and examined. In counting the number of nuclei in each cell Cooke's criterion should be kept in mind and the nuclear parts joined by more than a thread should be considered as one (see plate VII). Some experience is required in making the count because sometimes the lobes are lying in such a way that, although they may be separate, the whole looks like one convoluted lobe.

The normals.—Arneth gives the following figures as a normal count:

I	II	III	IV	V
5	35	41	17	2

If Cooke's criterion is adopted the normal reads as follows:

I	II	III	IV	V
10	25	47	16	2

The normal Arneth index (Bushnell and Treuholtz index) is about 60. In our work in asthma which we report below we have always made the count according to Cooke's method and have used the Bushnell and Treuholtz index (see page 257).

The value of the Arneth count in asthma

Not much attention has been paid to the Arneth count in asthmatic cases. Bray (1931) states that many observers during the crisis have recorded a change to the left in the Arneth count (Schiff noted this in thirteen out of fifteen cases) but he was not able to confirm this finding.

We have done the Arneth count in 143 cases of asthma, the results are tabulated in table I and above 70, out of 27 Gram-negative cases 19 have an index above 70, and out of 37 allergic cases

TABLE I
The Arneth indices in the three groups of asthma cases

Group	Total number of cases	Arneth index 60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
Bronchial	79	..	1	8	28	14	14	12	2
Gram-negative-bacilli group.	27	2	2	4	5	4	3	3	4
Allergic	37	5	8	8	7	3	2	2	2
TOTAL	143	7	11	20	40	21	19	17	8

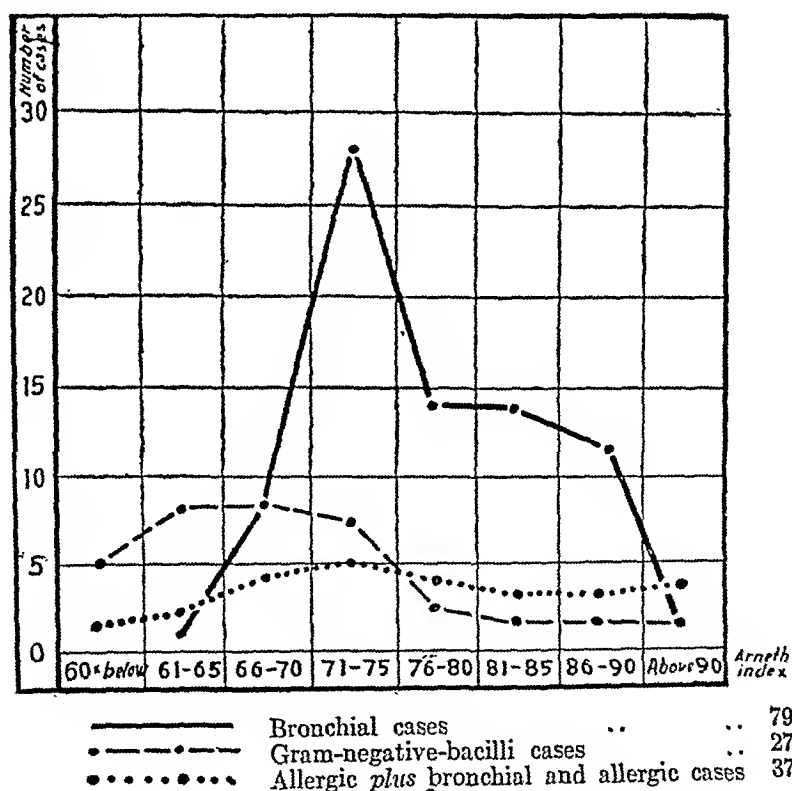
graph I. It will be seen that the index varies from below 60 to above 90 in different cases, the index being 60 and below in 7 cases, between 61 and 65 in 11 cases, between 66 and 70 in

21 have an index below 70, and only 16 above 70.

If the allergic group be further divided into true allergic cases and mixed bronchial and

GRAPH I

The Arneth indices in the three groups of asthma cases



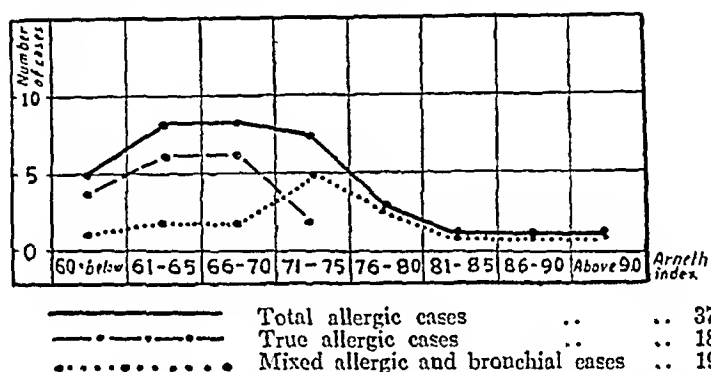
20 cases, between 71 and 75 in 40 cases, between 76 and 80 in 21 cases, between 81 and 85 in 19 cases, between 86 and 90 in 17 cases, and above 90 in 8 cases. Taken as a whole these figures give no information of any value. When the cases are divided into the three groups suggested by us (the bronchial group, the Gram-negative-bacilli group, and the allergic group) we find that the Arneth index is usually high in the bronchial and Gram-negative-bacilli groups and usually low in the allergic group. If we take 70 as the dividing line we see that out of 79 bronchial cases 70 have an index

allergic cases (table II and graph II) we see that out of the sixteen cases in this group with an index of above 70, 14 cases belonged to the mixed bronchial and allergic type and only two cases to true allergic type. These two allergic cases had an index of 71, so that for practical purposes all the true allergic cases have an index below 70. If the 19 mixed cases (bronchial plus allergic) be taken out of the allergic group and counted with the bronchial group we find that out of 98 cases only 14 have an index of below 70 and 84 cases have an index above 70. Of the 18 true allergic cases only two cases had an index above 70 (71). This

TABLE II
The Arneth indices in the allergic group of asthma cases

Group	Total number of cases	Arneth index 60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
True allergies ..	18	4	6	6	2
Mixed bronchial and allergic cases.	19	1	2	2	5	3	2	2	2
TOTAL	37	5	8	8	7	3	2	2	2

GRAPH II
The Arneth indices in the allergic group of asthma cases



is shown in table III. If the bronchial, the Gram-negative-bacilli, and the mixed bronchial

below, and the other class of bacterial cases containing the bronchial, the mixed bronchial

TABLE III

Group	Total number of cases	Arneth index 60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
Bronchial + mixed bronchial + allergic.	98	1	3	10	33	17	16	14	4
Gram-negative-bacilli	27	2	2	4	5	4	3	3	4
True allergic ..	18	4	6	6	2

and allergic cases be grouped together (table IV) we find that out of 125 cases only 22 cases have an index below 70 while 103 have an index above 70. By looking at table IV we can say that the asthma cases can be provisionally divided into two classes by means of the Arneth count—one class containing allergic cases in which the Arneth index will be 70 or

and allergic, and the Gram-negative-bacilli cases in which the Arneth index will usually be above 70. This latter class can be broken up into its component groups by means of the blood eosinophile count; we have shown in a paper which will shortly be published that the bronchial cases usually have a low eosinophile count; whilst the mixed bronchial and allergic

TABLE IV

Group	Total number of cases	Arneth index 60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
Bronchial, mixed and Gram-negative-bacilli cases.	125	3	5	14	38	21	19	17	8
True allergic cases ..	18	4	6	6	2

cases, the Gram-negative-bacilli cases and the allergic cases usually have a high eosinophile count. So that in summarizing we can state that :—

(1) The allergic cases usually have a low Arneth index and a high eosinophile count.

(2) The mixed bronchial and allergic cases with the Gram-negative-bacilli cases have often a high Arneth index and a high eosinophile count. The Gram-negative-bacilli cases can be separated from the mixed allergic cases by the presence of the Gram-negative-bacilli in the sputum.

(3) The bronchial cases usually show a high Arneth index and a low eosinophilia.

Conversely :—

(1) An Arneth index of below 70 is found in the allergic cases; this is usually associated with a high blood eosinophilia, but occasionally there is a low blood eosinophilia.

(2) An Arneth index of above 70 plus a low blood eosinophilia is usually found in the bronchial cases and not often in the mixed bronchial and allergic cases.

(3) An Arneth index of above 70 plus a high blood eosinophilia is usually found in the Gram-negative-bacilli cases, and in the mixed bronchial and allergic cases.

The total leucocytes and the Arneth count.—Tables V and Va show the relation between the total leucocyte count and the Arneth count. Table VI shows the relation between the total polymorphonuclear count and the Arneth count.

There are two groups of cases placed within heavy lines in table V that require some further explanation.

The first group consists of 16 cases with a leucocyte count of 13,000 to 37,000 per cubic millimetre showing no appreciable shift to the left. In other words in these cases a high leucocytosis is associated with a more or less normal Arneth count.

The second group consists of 31 cases with a leucocyte count of below 8,000 per cubic millimetre, with the Arneth count showing an appreciable or a very marked left-handed shift. In other words in these cases a leucopenia is associated with a marked shift to the left.

(1) *A high leucocytosis without any appreciable shift in the Arneth count.*—Table V shows that in all there were 45 cases with a leucocyte count of above 13,000 leucocytes per cubic millimetre of the blood. Out of these 45 cases there were 16 which had an Arneth index of below 70. Reference to table Va (p. 264) shows that out of these 16 cases eight belonged to the allergic group, four to the Gram-negative-bacilli group, and four to the bronchial group. We have shown that allergic and Gram-negative-bacilli cases as a rule have a high blood eosinophilia, some of the bronchial cases also have a high blood eosinophilia and the four bronchial cases referred to happened to have a high eosinophile count, so that we see that all the sixteen cases in this group had a high eosinophilia. The high leucocytosis in these cases is due to an increase in the numbers of eosinophiles, the number of polymorphonuclears remaining the same. We have plotted the total polymorphonuclears against the Arneth index in table VI. If we take the normal number of polymorphonuclears to be roughly 70 per

TABLE V
Arneth index

Total leucocytes under	60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90	
5,000	1	2	1	2	..	1	5
6,000	..	1	..	5	..	2	2	..	7
7,000	..	2	..	3	4	1	1	3	13
8,000	2	5	1	1	3	1	14
9,000	1	..	2	4	5	2	..	1	14
10,000	..	2	4	3	3	18
11,000	7	3	2	2	..	6
12,000	3	..	2	1	..	1	19
13,000	2	..	1	2	..	2
14,000	1	2	..	2	1	1	1	..	8
15,000	..	1	1	2	1	1	4	..	7
16,000	..	1	2	3	1	1	..	1	12
17,000	..	1	1	3
18,000	2	2	2
20,000	1	2	1	1	1	..	3
23,000	1	1	..	1	4
25,000	1	3
26,000	1	..	1	1
36,000	1
37,000	..	1	1
	7	11	20	40	21	19	17	8	=143

cent of the total leucocytes then a count of 13,000 leucocytes will roughly contain 9,000 polymorphonuclears. In table VI we find that

sixty-nine, out of these 69 cases as many as forty-five had an Arneth index varying from 71 to 90, i.e., showing a marked shift to the left.

TABLE VI
Arneth index

Total polymorphs under	60 and below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90	
2,000	3	1	1	1	..	6
3,000	2	4	1	1	2	3	3	..	16
4,000	1	4	3	8	2	1	2	2	23
5,000	2	1	4	7	4	1	3	2	24
6,000	2	3	1	4	1	2	13
7,000	1	1	2	5	4	2	4	1	20
8,000	3	3	3	1	10
9,000	1	1	1	4	2	2	2	1	14
10,000	1	1	1	1	1	..	5
11,000	2	2	..	1	5
12,000	1	1
13,000	1	1	2
14,000	1	1
15,000	1	1
16,000	1	1
17,000	1	1
18,000	1
19,000	1	1
20,000	0
	7	11	20	40	21	19	17	8	=143

there are 17 cases with a polymorphonuclear count of above 9,000 and that out of these cases there are only four with an Arneth index between 66 and 70, and the remaining 13 cases have an index varying from 71 to 90. This proves that a high leucocytosis combined with a low Arneth index means that the leucocyte increase is due to an eosinophilia.

(2) *The association of leucopenia with a high Arneth index, i.e., a marked shift in the Arneth count to the left.*—Table V shows that there were thirty-nine cases of this group who had a total leucocyte count below 8,000 per cubic millimetre of blood, out of these cases as many as thirty-one had an index of 71 and over. A reference to table Va shows that of these thirty-one cases, twenty belonged to the bronchial group, six to the Gram-negative-bacilli group, and five to the allergic group (these five cases were mixed bronchial and allergic cases). So that all the thirty-one cases in this group were associated with infection. Usually with a shift in the Arneth count to the left, i.e., with an active bone marrow we would expect to get a leucocytosis in the blood. In order to rule out the possibility of the leucopenia in these cases being due not to a decrease in the number of the polymorphonuclears but to a decrease in the other types of cells we have plotted the total polymorphonuclears against the Arneth index in table VI. If we take 5,000 polymorphonuclears in one cubic millimetre of blood to represent roughly the normal figure we see in table VI that the number of cases who had a polymorphonuclear count of below 5,000 was

So that we see that in these cases there is a polymorphonuclear leucopenia and yet a shift in the Arneth count to the left indicating that in spite of the reduction of polymorphonuclear cells in number—young forms are in preponderance.

Cooke (1928) maintains that in all cases of microbic infection there is a left-handed shift in the Arneth count whether the total polymorphonuclears remain normal in number, whether there was a polymorphocytosis or whether there was a polymorphopenia. A shift to the left in the Arneth count with a polymorphopenia therefore must mean that the activity of the bone marrow cannot keep pace with the destruction of these cells. In the tropics many of these cases are subjects who have malaria, kala-azar or hookworm infections.

Piney (1927) is of the opinion that when an infection is intense it depresses the bone marrow and causes a neutrophile leucopenia instead of the usual neutrophile leucocytosis, the latter is characterized by a shift to the left in the Arneth count. In those cases where there is a neutrophile leucopenia with a shift to the left in Arneth's count he considers that there is some toxic agency causing a complete alteration in the process of maturation of the neutrophilic cell.

Ponder (1926) stated the equilibrium in the percentage of cells in the various Arneth classes was in no way dependent on the number of

cells in the blood stream. The only essential thing for this equilibrium is that the number of cells entering the circulation be equal to the number leaving it. He discusses all the possible combinations between the rate of production of the polymorphonuclear cells and their removal from the blood stream.

TABLE Va
Arneth index

Total leucocytes under	60-Below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
5,000	1				1	2		1
6,000		1		1	1	2	1	
7,000			1	2		1	2	
8,000		1		1	4	1	1	2
9,000	1		2	2		1	2	1
10,000		2	2	1	1	2		1
11,000	2		2	7	3	2	2	
12,000	1			1		1		
13,000		2		1		1	2	
14,000	1	1	1	2	5			
15,000			1	2		1	3	
16,000		1	1	2	1	1	3	
17,000			1					1
18,000	1			1				
20,000			1		1	1	1	
23,000						1		
25,000			1					1
26,000				1		1		
36,000		1						
37,000								

1. (ordinary type)=Bronchial cases.

11. (out-lined figures)=Gram-negative-bacilli cases.

1. (bold-face figures)=Allergic plus bronchial and allergic cases.

We can thus appreciate (a) why a leucocytosis with a normal or sub-normal Arneth's count is seen in asthmatics—and it is due to a

high eosinophilia, and (b) why, when there is a leucopenia, there is still a shift to the left in the Arneth count.

REFERENCES

- Arneth, J. (1904). *Die Neutrophile Weissen Blutkarperscheran*. Jena. Fisher.
- Bray, G. W. (1931). *Recent Advances in Allergy*. London: J. & A. Churchill.
- Bushnell, G. E., and Treuholtz, C. A. (1908). *Med. Record*, Vol. LXXIII, p. 471.
- Charipper, H. A. (1929). *Quart. Journ. Exper. Physiol.*, Vol. XIX, p. 109.
- Climenko, D. R. (1930). *Quart. Journ. Exper. Physiol.*, Vol. XX, p. 193 and p. 370.
- Climenko, D. R. (1932). *Quart. Journ. Exper. Physiol.*, Vol. XXII, p. 25.
- Colbert, C. N. (1924). *Journ. Lab. and Clin. Med.*, Vol. X, p. 126.
- Cooke, W. E. (1914). 'The Arneth count'. Glasgow.
- Cooke, W. E. (1928). *Lancet*, Vol. II, p. 1040.
- Danzer, M. (1930). *Quart. Journ. Exper. Physiol.*, Vol. XX, p. 141.
- Egloff, A. (1926). *Zeitschr. Klin. Med.*, CIII, 411.
- Fleming, G. W. T. H. (1929). *Brit. Med. Journ.*, Vol. I, p. 638.
- Hamilton-Black, E. (1913). *Brit. Med. Journ.*, Vol. I, p. 113.
- Holroyd, J. B. H. (1913). *Brit. Med. Journ.*, Vol. I, p. 927.
- Hunt, E., and Weiskotten, H. G. (1930). *Amer. Journ. Path.*, Vol. VI, p. 175.
- Kennedy, W. P., and Grover, C. A. (1928). *Quart. Journ. Exper. Physiol.*, Vol. XVIII, p. 79.
- Kennedy, W. P., and Flint, K. N. (1930). *Quart. Journ. Exper. Physiol.*, Vol. XX, p. 101.
- Kennedy, W. P., and Thompson, W. A. R. (1929). *Quart. Journ. Exper. Physiol.*, Vol. XIX, p. 377.
- Kennedy, W. P., and Thompson, W. A. R. (1928). *Quart. Journ. Exper. Physiol.*, Vol. XVIII, p. 263.
- Lim, R. K. S., Sarkar, B. B., and Brown, J. P. H. G. (1922). *Journ. Path. and Bact.*, Vol. XXV, p. 228.
- Piney, A. (1927). *Recent Advances in Haematology*. London: J. & A. Churchill.
- Ponder, E. (1924). *Quart. Journ. Exper. Physiol.*, Vol. XIV, p. 327.
- Ponder, E. (1926). *Quart. Journ. Exper. Physiol.*, Vol. XVI, p. 227 and p. 241.
- Ponder, E. (1928). *Quart. Journ. Exper. Physiol.*, Vol. XVIII, p. 127.
- Ponder, E., and Flinn, Z. M. (1926). *Quart. Journ. Exper. Physiol.*, Vol. XVI, p. 207.
- Ponder, E., and Flint, K. N. (1926). *Quart. Journ. Exper. Physiol.*, Vol. XVI, p. 225 and p. 393.
- Ponder, E., and Flint, K. N. (1928). *Quart. Journ. Exper. Physiol.*, Vol. XVIII, p. 45.
- Pons, C., and Krumbhaar, E. B. (1924). *Journ. Lab. and Clin. Med.*, Vol. X, p. 123.
- Roberts, K. (1927). *Amer. Journ. Surg.*, Vol. III, p. 223.
- Schilling, V. (1920). *Ztschr. f. klin. Med.*, 89, 1.
- Weiskotten, H. G., Schwartz, S. C., and Steensland, H. S. (1915). *Journ. Med. Res.*, Vol. XXXIII, p. 127.
- Weiskotten, H. G., and Steensland, H. S. (1919). *Journ. Med. Res.*, Vol. XXXIX, p. 485.
- Weiskotten, H. G., Wyatt, T. C., and Gibbs, R. F. D. (1924). *Journ. Med. Res.*, Vol. XLIV, p. 593.

NOTES ON BERBERINE SULPHATE IN ORIENTAL SORE

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DURING the last few years a number of papers on the treatment of oriental sore by berberine sulphate have appeared in the *Gazette*. As in most instances only a small number of cases have been reported upon, it was suggested to the writer that in Rajputana, where the disease is endemic, it might be possible to collect notes of the results of treatment in a large series of cases.

Berberine sulphate has been used as one of the standard treatments for oriental sore for the last two years. The method adopted has been that suggested by Das Gupta (1930), namely, the impregnation of the sore and the tissues immediately adjacent to it, both at the base and around the edges, with a one or two per cent solution of acid berberine sulphate.

The details that it has been possible to collect are regrettably incomplete. It is almost impossible, even in big hospitals, for medical officers to keep detailed notes of out-patient treatments, in view of the mass of work which each man has to get through, often under very unsatisfactory conditions as regards accommodation; the same remark applies even more forcibly in country districts, where there is one doctor to 100,000 people spread over an area of 2,000 square miles.

Again, it will be seen that the majority of the cases are diagnosed clinically. It is of course very desirable that in every case the diagnosis should be confirmed by microscopical examination, but this is a degree of perfection that it is almost impossible to achieve under the present conditions. However, the sore has certain very marked characteristics with which medical officers working in an endemic area are usually familiar. A negative finding is by no means conclusive evidence against the diagnosis of oriental sore; therefore the finding of leishmania in about one in four of the State hospital cases suggests that a very large percentage of the cases are really oriental sore.

The details collected from three sources are given below.

District dispensary cases

Thirty-nine patients were treated, 3 on positive laboratory diagnosis and 36 on clinical diagnosis, with complete cure in all cases. One hundred and seventy-five injections in all were given, the average being therefore $4\frac{1}{2}$ injections per patient.

In 8 more clinically-diagnosed cases, a total of 26 injections was given; these patients showed definite improvement but failed to complete the course of treatment.

In 14 other cases, 24 injections in all were given, but as the patients did not attend again no prognostic observations were made.

City dispensary cases

Fifty cases, diagnosed clinically, were all reported cured after an average of 5 injections each. No details are obtainable.

State hospital cases

Three hundred and ninety-eight cases were examined microscopically; in 140 of these leishmania was found. Of the 398 patients, 264 consented to injections being given; these included 79 cases in which leishmania had been found, the remainder being clinically diagnosed.

In all 611 injections were given as follows:—

Cases in which 1 injection was given ..	132
" " " 2 injections were given ..	51
" " " 3 " " " ..	35
" " " 4 " " " ..	14
" " " 5 " " " ..	13
" " " 6 " " " ..	11
" " " 7 " " " ..	2
" " " 8 " " " ..	1
" " " 10 " " " ..	1
" " " 13 " " " ..	3
" " " 14 " " " ..	1

All those who received five or more injections were definitely cured. Those who received three and four all showed some improvement. Of those who only attended once, nothing more is known, and nothing definite can be said of those who only attended twice.

The above records are of only limited value, in my opinion, but they indicate that the injections are sufficiently painful to drive a very large number of patients away.

However, educated patients, who understand the necessity for the injections, and patients that can be persuaded by the local doctor, who in country districts is often in close touch with the people, continue the treatment and reap the benefit, as it would appear that, if persevered with, berberine sulphate injections are a certain cure in cases of oriental sore and also possibly of other sores.

REFERENCE

Das Gupta, B. M. (1930). The treatment of oriental sore with berberine acid sulphate. *Indian Med. Gaz.*, Vol. LXV, p. 683.

AN ACCOUNT OF THE EPIDEMIC OF CEREBRO-SPINAL FEVER IN THE BORSTAL INSTITUTION

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An epidemic of cerebro-spinal meningitis broke out in the Borstal Institution, Lahore, suddenly during the spring of 1932. The first two cases occurred on 12th March and cases continued to occur at varying intervals right up to the middle of June, a total of eighteen cases

in all. Subsequent to this no cases occurred for a period of about two and a half months, when suddenly at the end of August there was a fresh outbreak with four seizures up to the date of this report, November 1932.

Before giving a description of the various features of the epidemic it would be useful to give brief information about the conditions prevalent in the institution prior to the outbreak of the epidemic. This institution is primarily meant to accommodate adolescent and juvenile offenders. The designed accommodation provided is for 1,705 inmates. Out of these 350 inmates live in 'association barracks' and the remainder in single cells.

The actual population at the time of the outbreak was 1,721, and for the preceding four months it had ranged between 1,800 and 2,489. About the middle of November 1931, owing to the Ahrar movement, a very large number of prisoners were received for admission in this institution; these had been evacuated from various camp jails of Kashmir State, *e.g.*, those at Satwari, and Udhampur. Though no authentic information is available of the occurrence of any case of cerebro-spinal fever in the camp jails in Kashmir, which were seriously overcrowded at the time for unavoidable reasons, yet some of the prisoners received from there mentioned the occurrence of an illness somewhat similar in nature to the present seizures. It is quite possible that the overcrowding in these camp jails may have led to an increase in the percentage of carriers amongst the population confined therein. The present epidemic in the Borstal Institution may be the direct outcome of increase of carriers brought about by the arrival of a large number of carriers amongst the prisoners received from the Kashmir State.

Mode of spread

The first two cases occurred amongst the inmates working in the kitchen, and at intervals isolated cases cropped up like mushrooms with surprising suddenness from different circles and barracks. It was very difficult to establish the connection of one case with another; while one inmate fell a prey to the disease his close associates entirely escaped. The disease in most cases picked out those inmates that were apparently healthy and well nourished. None of the established carriers (detected by examination of throat swabs) and none of the hospital staff or attendants contracted the disease.

Signs and symptoms

Out of the twenty-two cases that have occurred up to date five were of the fulminating type, and the rest may be labelled as of acute type. A brief description of each type is given below.

Fulminating type.—Cases of this type when brought to the hospital were invariably unconscious and deeply comatose. History was forthcoming from the comrades of the patient that he had been complaining of slight headache and slight fever prior to unconsciousness. The patient kept in a state of active delirium, very restless, giving forth every now and then a short monosyllabic cry. The eyes were rolled up with corneæ insensitive and with reflexes, both superficial and deep, invariably lost. Incontinence of urine and faeces was present in most of them. Rigidity and Kernig's sign were absent. Limbs were flaccid. Cerebro-spinal fluid was slightly purulent in some cases, and in others it was so thick that it could hardly be drawn. These patients invariably died, the whole course of the disease lasting a few hours.

Acute type.—Patients on admission complained of fever with rigors, severe headache, vomiting, rigidity of the neck, etc. One noticed impaired mental condition in most of them. They were dull and apathetic, and their reflexes both superficial and deep were either totally absent or sluggish. Some of the patients had marked hyperæsthesia; so much so that they gave forth a sharp cry whenever they were touched.

Two cases exhibited very mild features. There was complete absence of any abnormal mental conditions, and pyrexia was slight and of short duration. The only sign noticed was rigidity of the neck.

It will be useful to put down for information the salient features of the various signs and symptoms observed in these cases.

Fever.—The pyrexial period varied from four days in one case to twenty-six days in another, the average being twelve days. In many cases there was a recurrence of temperature after several days of apyrexia and in most of the cases this coincided with some complication, such as affection of the joints. No special peculiarity has been noticed as characteristic of this disease. Fever charts of a few cases are given on page 269.

Rigidity of neck and back.—This was a marked and common feature found in practically all cases excepting the fulminating type. The degree of rigidity varied in different cases; in the majority of cases it was simply complained of as stiffness of neck or muscles of the back. In two cases it was of extreme severity, the patients being practically rigid like a board and in an opisthotonic condition for a period of forty-eight to seventy-two hours. Repeated drawings of cerebro-spinal fluid afforded relief in a large number of cases, but made little or no difference in severe cases.

Headache.—Headache in varying degrees of severity was complained of in all cases. A history of the presence of headache was obtainable in all the cases before the onset of other symptoms; in some cases it was complained of as lancinating in character. Repeated lumbar punctures gave considerable relief. Persistence

of headache for several weeks even after apparent recovery was a common feature in all cases.

Herpes.—Herpes developed in 50 per cent of cases; in all the cases it was extensive. In seven cases it involved the area of lips and cheeks and in two it appeared on the sides of chest. It usually appeared about the end of the first week but in some cases as early as the second day of illness.

COMPLICATIONS

Joint affections.—This complication arose in four cases of the series during the second week of the illness. Two cases showed involvement of knee joints with a good deal of effusion in the synovial cavity accompanied by other signs very much like acute arthritis. The fluid aspirated from the knee joint was a pale exudate, thick and gelatinous in character. Microscopic examination revealed the presence of a large number of pus-cells but no meningococci. Cultures from the joint effusion were reported to be negative for meningococci. In the other two cases the affection consisted of acute arthralgia of the knee.

In cases of involvement of the knee joint accompanied by effusion, repeated aspirations and injections of 10 cubic centimetres of anti-meningococcus serum into the joint resulted in rapid improvement and disappearance of symptoms.

Hemiplegia.—This occurred in one case only, on the 12th day of the disease. The right upper and lower extremities were both involved. It was not progressive but came on suddenly. This patient eventually died three days after the appearance of paralytic symptoms.

Diplopia.—This was observed in one case only. It occurred on the twenty-sixth day of illness, viz, during convalescence. It lasted for eight days and then gradually disappeared altogether.

Pneumonia.—This occurred in one case only. It was of the lobar type, and appeared on the second day of the illness; it proved rapidly fatal, the patient dying on the same day.

Diagnosis

In an institution with a population of about 1,700 inmates it was very important to discover and diagnose cases of cerebro-spinal fever as early as possible, both with a view to arresting the further spread of the epidemic, and to giving early treatment, thereby increasing the chances of recovery. Cases presenting even the slightest signs clinically were promptly segregated in a separate hospital reserved for them inside the institution. To achieve the object of early diagnosis, the following procedure was adopted as a routine in examination of the cases:—

Blood examination.—Blood films of all such cases that were admitted in the institution hospital with pyrexia were carefully examined with a view to detecting the presence of (a) any

blood-parasites and (b) a polymorphonuclear leucocytosis. Cases which presented a blood picture of polymorphonuclear increase to 80 per cent or more were marked for special observation for any subsequent development of clinical signs, e.g., headache, rigidity of the neck, or Kernig's sign. This procedure was found a good aid to early diagnosis of cases.

Lumbar puncture.—This was performed in all cases whether clinically positive or suspicious. In cerebro-spinal-fever cases the fluid came out under great pressure and was turbid—the turbidity varying from slight opalescence in less severe cases to a purulent exudate in the fulminating cases. It is interesting to note that in one fulminating case from the very beginning no cerebro-spinal fluid could be drawn in spite of repeated punctures; this patient died within a few hours. In two other cases failure to draw any fluid from the cerebro-spinal canal occurred at a later stage of the illness. Microscopic examination of cerebro-spinal fluid invariably revealed the presence of enormous numbers of polymorphonuclear leucocytes and a few intracellular diplococci morphologically indistinguishable from meningococci. A specimen of the same fluid drawn was sent for cultural examination to the bacteriological laboratory of the King Edward Medical College, Lahore, which reported the results as 'positive', in all cases. All the specimens of cerebro-spinal fluid in positive cases showed absence of glucose and increase of albumen.

Pathological autopsies

Out of eleven patients that died of cerebro-spinal fever, three were sent to the King Edward Medical College for post-mortem examination. For detailed post-mortem reports see appendix.

TREATMENT

Serum therapy.—Immediately a case was diagnosed as cerebro-spinal fever, anti-meningococcus serum (20 to 30 c.cm.) was administered intrathecally and about 10 to 20 cubic centimetres intravenously. In all the acute cases intrathecal administration was repeated practically every twenty-four hours, until the patient's condition showed improvement and the cerebro-spinal fluid was found to be free from meningococci.

The two indications taken as guiding factors for further administration of serum were (a) the patient's general condition and (b) the condition of the cerebro-spinal fluid. Mere opalescence or slight turbidity of the cerebro-spinal fluid was not considered a sufficient indication for a further dose of serum. Administration of serum was suspended only at the stage when the cerebro-spinal fluid showed absence of meningococci and a return of the presence of sugar. On an average 100 to 150 cubic centimetres of anti-meningococcus serum per head was found to be sufficient in our cases;

the maximum amount of serum required in one case was 225 cubic centimetres.

Lumbar puncture

Lumbar puncture in addition to being a necessary concomitant of intrathecal administration of serum was performed whenever the necessity arose for relieving the pressure symptoms. The quantity drawn at each sitting varied in different cases; in one case 95 cubic centimetres of cerebro-spinal fluid was drawn at one sitting alone. During the course of treatment dry punctures were met with in three cases. In one case after successive dry punctures on three consecutive days, there was a return of cerebro-spinal fluid on the fourth day. This patient is still under treatment and is doing well.

Prophylactic measures

While devising and putting into practice the measures to combat the propagation of this disease one had to keep in view the fact that the meningococcus is an inhabitant of the nose and nasopharynx, that the disease is by droplet infection, and that for all infections of this sort a close contact is generally necessary as the meningococcus is an organism of very low vitality which cannot stand the extremes of temperature, daylight, or desiccation for long, and whose life outside the body is amazingly short. The delicacy of the organism strongly suggests that the disease is spread directly from an individual who is harbouring the virus whether he be a patient suffering from the disease, a mild abortive case going about unnoticed in the community, or a carrier. Keeping the above facts in view the following prophylactic measures were carried out:—

Isolation of the sick.—All cases of cerebro-spinal fever were promptly isolated in the hospital in the new section of the Borstal Institution, so that there was no chance of anybody having access to them except the hospital attendants.

Segregation of the contacts, and carriers.—The contacts of these cases were promptly segregated and each of them was kept in a separate cell. Their throats were examined to detect carriers among them. During the day they were made to work in the open air and every contact was under the close observation of the medical staff.

The nasopharynxes and throats of all the inmates, including the contacts, were examined and swabs taken to detect carriers of meningococci amongst them. The carriers were kept separate from the others and were made to work in the open air during the day-time. They too were under close observation of the medical staff.

To detect new cases as early as possible all the fever cases were examined twice daily, in the morning and evening, and instructions were issued to bring promptly to the notice of the medical staff any patient complaining of severe headache, fever, catarrh, etc.

Avoidance of overcrowding.—Existing berths in the association-barracks being considered too close to each other in most cases, it was ordered that the inmates should sleep on alternate berths. They were advised to sleep with their heads against the iron gratings to get more fresh air.

Overcrowding was avoided in the workshop by keeping the men sufficiently apart from each other and making them work as far as possible in open air.

School classes were held in the verandahs or open air.

Prisoners working in the kitchens were gradually replaced and put on outdoor work.

To reduce the humidity of the cells and barracks all *lipai* and *pocha* was prohibited.

Disinfection of clothing and equipment of the inmates

All the blankets and clothes were disinfected by passing through a pressure steam sterilizer.

All blankets and mats during the day were spread out in the sun.

Chlorine solution was supplied to enable the inmates to soak their safas in it, as these are usually used as towels for cleaning their noses.

The use of common drinking vessels by prisoners was strictly prohibited.

Lectures were delivered to the inmates on the importance of scrupulous cleanliness of their persons and clothing, and on the dangers of haphazard spitting, sneezing and coughing in presence of other inmates.

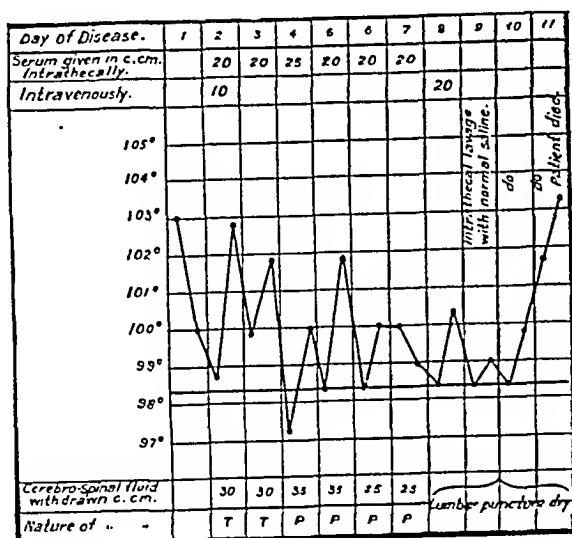
Phenyle cups were provided in the institution at various places, and the importance of spitting into them *only* was impressed on the inmates and the staff.

Gargling parades were held at lockout and lockup time to administer Condyl's fluid as gargles to the inmates.

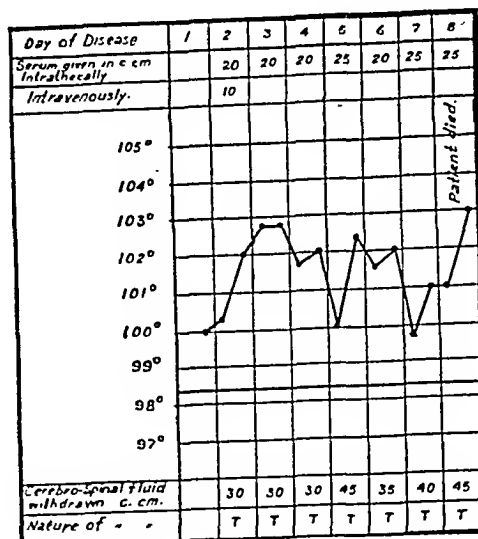
Visitors were reduced to a minimum, and the interviewers were made to interview the prisoners at a distance of at least three feet from them.

Admissions to the institution were stopped for the epidemic period.

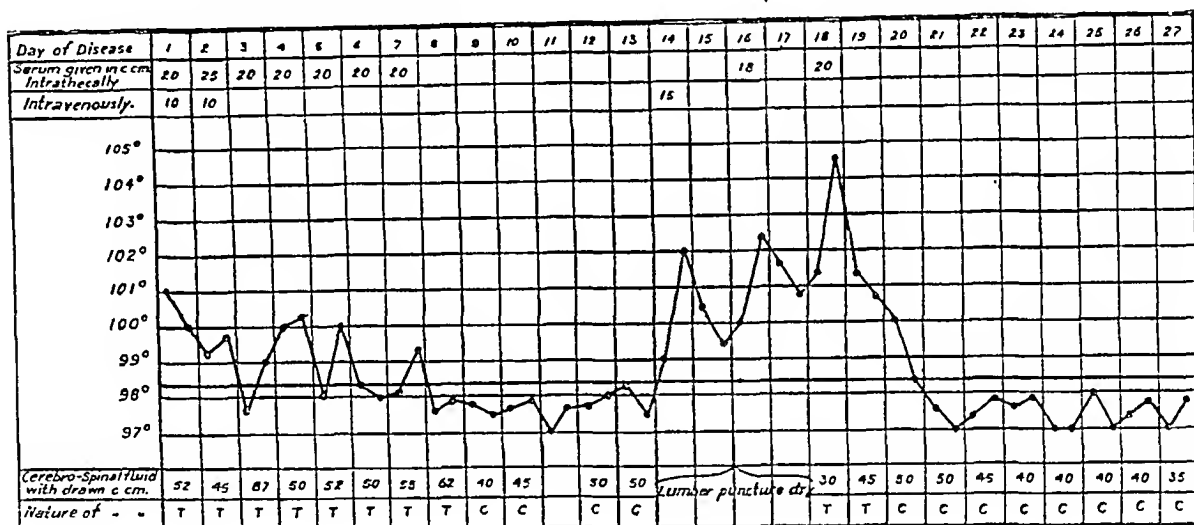
In addition to the above measures the general sanitation of the institution was scrupulously looked after and every barrack and cell was whitewashed and disinfected.



I. A fatal case.
(T = turbid; P = purulent).



II. A fatal case.
(T = turbid).



III. A non-fatal case.
(T = turbid; C = clear).

APPENDIX

Autopsies

Case 1. Nervous system.—The sub-arachnoid in the entire cerebro-spinal axis full of yellow pus. No distension of ventricles. Pus showed Gram-negative diplococci resembling the meningococcus.

Respiratory system.—Both lungs showed parietal adhesions. Left lower lobe collapsed and firmly adherent to chest wall. It had to be torn away piecemeal in removal. Trachea congested.

Abdomen.—Slight enlargement of mesenteric lymph nodes. Gastric mucosa acutely congested. Mucosa of intestine congested with submucous hæmorrhages at places.

Spleen.—Enlarged. Acutely congested causing a diffuent condition of the pulp.

Liver.—Showed yellow areas of necrosis.

Kidneys.—Acutely congested.

Case 2. Nervous system.—Marked congestion of superficial blood vessels. A purulent exudate at the base and on the posterior aspect of the spinal cord. Ventricles greatly distended with turbid fluid as the result of

internal hydrocephalus. Smears from pus showed meningococci.

Kidneys.—Hyperæmic.

Case 3. Nervous system.—Intense engorgement of surface blood vessels. No sub-arachnoid accumulation of the pus on vertex. Marked degree of purulent meningitis at the base. Pus smears from the base showed intracellular diplococci in a predominantly polymorphonuclear exudate.

Respiratory system.—Left lung showed firm parietal adhesions. Hypostatic congestion in both lungs.

Circulatory system.—Pericardium contained about three ounces of hæmorrhagic effusion. Heart flabby. No gross surface abnormality.

Abdomen.—Two areas of submucous hæmorrhages in the intestine, one high up in the ileum, the other in ascending colon.

Spleen.—Enlarged. Trabecular hypertrophy. Diffuent owing to decomposition.

Liver.—Atrophied. Surface mottled but smooth. Section showed numerous regenerating nodules as seen in toxic cirrhosis.

SPINAL PERCAIN ANÆSTHESIA

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PERCAIN, a derivative of quinoline, is far more powerful in its action than any of the cocain and novocain group of drugs, and, though it is also far more toxic, its toxicity does not matter for practical purposes, owing to the extreme dilution in which it is used for spinal anæsthesia.

A preliminary injection of morphia (1/6th to $\frac{1}{4}$ gr.) and liyoscine (1/150th gr.) should be given half an hour or so before the spinal anæsthetic is administered. In a very nervous patient a light chloroform anæsthesia can be given for the spinal injection, or the skin over the lumbar spines can be rendered anæsthetic with novocain.

A solution of 1 part of percaïn in 1,500 parts of 0.5 per cent sodium chloride is used. This solution must be sterilized and tested with litmus or phenolphthalein, and if it is alkaline it must be neutralized with a drop or two of dilute hydrochloric acid, as it does not keep in an alkaline solution.

The syringe for its use, together with the spinal needles, must be washed out with sterile distilled water, or a precipitate will form. An average dose is 9 c.cm. of this solution, and it is injected fairly rapidly into the cerebrospinal canal at the level of the interval between first and second, or second and third lumbar vertebræ, the patient lying in the usual position on the side with head and knees approximated so as to arch the back.

Owing to the solution (specific gravity 1003.5) being lighter than cerebrospinal fluid (specific gravity 1005.5) the patient must at once be placed in the ventral decubitus on a flat table, with the head slightly inclined downwards projecting over the end of the table. The patient must remain in this position until sensation is absent up to about the level of the seventh or eighth dorsal nerves; this may take from six to ten minutes. He is then turned into the position of dorsal decubitus, the head still being kept low. The operation may now begin.

A considerable lowering of the blood-pressure will by this time have taken place, but although this may be restored by the injection of advenalin or ephedrine, we have found it in almost every case quite unnecessary to do this. Patients have remained throughout a long operation with a blood-pressure of between 40 and 60 millimetres of mercury without any apparent ill-effects, and we now hardly ever take any notice of the blood-pressure, though the anæsthetist ought to feel the pulse from time to time as a precautionary measure.

The operation can be performed with an almost total absence of shock, a very striking absence in big operations, such as abdomino-

perineal cancer of rectum, Wertheim's hysterectomy, or gastrectomy.

For gastrectomy we usually give a splanchnic anæsthetic as well, as soon as the abdomen is opened, injecting 30 cubic centimetres of 0.75 per cent novocain into the prevertebral space at the level of the first lumbar vertebra. The immediate effect of this is to raise the blood-pressure, sometimes almost to the normal. Moreover it prevents the reflex retching and vomiting which otherwise may occur when the stomach and upper abdominal viscera are manipulated.

The anæsthesia is usually complete for some two hours, though the time varies considerably and may be as long as three and a half hours. For this reason, the patient when put back to bed should have his head kept low, without a pillow, and the foot of his bed raised six inches or so until three hours after the end of the operation.

We have done at Neyyoor some one hundred and fifty cases by this method of anæsthesia during the last few months, and now use it invariably for all operations on the abdomen and most others on the lower half of the body. Complications are usually of little significance, and may be tabulated as follows, in order of frequency.

(1) Rise of temperature varying from 1° to 6° (or in one case 7°), lasting a few hours, and of no apparent influence on the patient's recovery and convalescence.

(2) Headache, beginning a few hours after the operation, and lasting for a time varying from three hours to three days. Usually the headache is slight, but in three or four cases it has been severe, and in one case it was very severe indeed.

(3) Restlessness, lasting one or two days, in six cases of our series. In only two cases was this serious, and both of them recovered without any further mishap.

Beyond these we have not seen any complications at all. But doubtless if the head and neck are not kept low we would have had to record failure of respiration. The lower intercostal muscles are of course paralysed in every case, but the diaphragm makes up for their inaction; it is however important to take postural precautions that the diaphragm be not paralysed.

The absence of irritating effects on the lungs is an important advantage of this method of anæsthesia; but the most striking benefit from its use is the total absence of vomiting after abdominal operations. Percain anæsthesia enables big operations to be performed in cases that are otherwise inoperable or desperate, with a minimum of risk; and we have often been surprised at the extreme fitness of patients after extensive operations. It is no exaggeration to say that a gastrectomy with percaïn anæsthesia gives us less trouble and anxiety after operation than a gastro-enterostomy used

to do with inhalation anæsthesia. I recently did a perineal excision of a rectum in which the patient was as fit after the operation as is the average case of hydrocele. Another great advantage of percain anæsthesia is the excellent relaxation of the abdominal muscles, which renders closure of the wound extremely easy, and exposure of the viscera is far more readily obtained than it ever is with even the most skilfully administered inhalation anæsthetic. A short time ago I removed an appendix through a gridiron incision with no assistance and no anæsthetist, and nobody to hand instruments or thread needles, in less than a quarter of an hour. I found the retraction of the muscles and the subsequent closure of the wound very easy to do. I do not recommend this procedure to any surgeon, but it shows what percain can do, and suggests its utility in an emergency when sufficient help is unobtainable or where the technique or sterility of assistants cannot be trusted.

A word of warning must be given with regard to failure to produce anæsthesia. This has happened several times in our series, but in only one case has it occurred where the cerebrospinal fluid dropped freely from the spinal needle on insertion. If the flow of fluid be not free, or if the fluid is stained with blood, it is probable that the opening at the point of the needle is only partially in the subarachnoid space. The remaining part may be between the dura and arachnoid membranes (in the subdural space) or leading into a blood-vessel. In these circumstances only a portion of the percain solution will be injected subarachnoidally, the remainder having no anæsthetic effect. And of the failures to produce anæsthesia which we have seen, this was the apparent reason in every case except the one already mentioned. It may therefore be taken as practically universally true that every case in which a satisfactory flow of clear cerebrospinal fluid is seen through the needle before the injection is done will be successfully anæsthetized by percain, provided the technique is carried out as described, and the right amount of the solution injected. For an average adult male, 9 to 10 cubic centimetres are sufficient to produce anæsthesia up to the sixth dorsal nerve. Short patients require less (7 c.cm. or so) and patients with a very long vertebral column may require up to 11 cubic centimetres.

In conclusion, it may be said that percain spinal anæsthesia as described is as far as is at present known the ideal anæsthetic for all abdominal and lower extremity operations, is pleasant for both the patient and the surgeon, and reduces the distress from vomiting and the risks from other complications to the minimum to which modern science can at present reduce them.

The analysis of one hundred consecutive cases shows the following figures :—

Headache was severe in two, bad in nineteen, slight in sixteen, and absent in sixty-three cases.

Restlessness was severe in one and moderate in three cases.

Shock occurred in two cases.

Pneumonia followed in seven cases (all this series were done at a bad time of year for pneumonia).

Vomiting after operation in five cases, two of which were abdominal cases.

Drop in blood-pressure.—The largest falls were from 110 to 30 millimetres, *i.e.*,—80 millimetres, and from 140 to 50, *i.e.*,—90 millimetres; the average was 42 millimetres in the whole series.

Failure.—Percain failed to act, though cerebrospinal fluid was freely obtained, in one case.

Deaths.—None were directly due to percain. One patient died of anæmia and one of uræmia, each four days after operation; one died of dysentery, fourteen days after operation.

Operations represented

Gastro-enterostomy	..	52
Gastrectomy	..	9, with one death.
Appendicectomy	..	8
Hernia and hydrocele	..	10
Hysterectomy	..	3
Excision of tuberculous		
cæcum	..	5, with one death.
Other cases	..	13
		<hr/> 100

OBSERVATIONS ON AN EPIDEMIC OF WHOOPING-COUGH AT THE LAWRENCE ROYAL MILITARY SCHOOL, SANAWAR

WITH A NOTE ON THE INVESTIGATION OF A SKIN REACTION IN THIS DISEASE

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and

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THE following observations were made on a series of 25 cases of whooping-cough occurring at the Lawrence Royal Military School, Sanawar, between 29th July and November 1932.

Previous epidemics

It will be of interest first to tabulate the month of the year in which previous epidemics of whooping-cough in this school commenced :—

TABLE I

1897 .. January	1912 .. May	1929 .. March
1898 .. July	1913 .. March	1930 .. May
1905 .. April	1914 .. February	1932 .. February
1907 .. June	1915 .. March	1932 .. July

This table shows that there is no very definite seasonal incidence.

The present epidemic

In the epidemic under consideration, the infection was brought to the school from Kasauli by a member of the boys' department, where three further cases occurred. One of these patients transmitted it to the preparatory department which he was attending daily for class-work, here it spread extensively, though no further cases occurred in other departments. (This chain of infection is a good illustration of an important axiom of school-hygiene, viz, that the separate departments in a large school should be kept as isolated as possible from each other.) One case occurred in a sweeper's child.

The preventive measures adopted consisted of:

- (a) Complete segregation of all four departments.
- (b) Lessons in the preparatory department being conducted in the open air.
- (c) The use of 'Izal' disinfectors, especially in chapel, which was attended by both boys and girls.

It was impossible to attempt to isolate children in the preparatory department in the catarrhal stage, practically all of them having coughs owing to the wet weather.

Mode of infection.—The mode of infection is shown by the following table:—

TABLE II

Infected from dormitory neighbour	.. 1
Infected from class neighbour	.. 7
Infected from playmate	.. 13
Infection not directly traceable	.. 4

This table shows the importance in epidemics of finding out from house-masters, etc., the names of the friends of infected children.

Incidence.—Among the cases in the preparatory department, where both sexes were equally exposed to infection, 13 boys and 7 girls were affected. No true deduction can be made regarding age incidence, as the majority of the cases were amongst children of a selected age. Weakly children and those with unhealthy tonsils did not appear to be especially prone either to infection or to severe attacks.

Characters of the epidemic.—The average whooping period was found to be 13.52 days; the longest period was 46 days, whilst in three cases no whooping occurred, the diagnosis depending on the occurrence of a catarrhal stage followed by vomiting.

Vomiting occurred at some stage in every case; in nine cases it preceded the whoop by one to eight days, and in six cases it outlasted the whooping stage by one to eight days. In ten cases the temperature reached 100°F. or over, three of these being weaklings. In ten cases, rales were noted in the chest.

Relapses occurred in six out of twenty-five cases, three patients having a double relapse.

One relapse was characterized by vomiting only. Five out of the nine relapses occurred shortly after a heavy fall of rain (2.5 inches), when the humidity was high and there was little sunlight for the patients to play in.

The following complications were noted: broncho-pneumonia (1), otitis externa (3), pyelitis (1), tonsillitis (2), severe sub-conjunctival hæmorrhage (1), and prolapse of rectum (1). The last is better described as a sequela. It occurred during the third short relapse in a debilitated patient, aged 3.

There is little doubt in the writers' minds that, in the light of the epidemic under review, a progressive immunity develops in a group of individuals exposed to infection, and that immunity to whooping-cough can be acquired without the individual necessarily suffering from any symptoms. The reasons for this conclusion are as follows:—

(1) The whooping stage towards the close of the epidemic became far shorter than the average; in the last four cases it was absent in two, and lasted one and two days, respectively, in the other two.

(2) Among four nurses, aged 17 to 19, who had not had whooping-cough and who were in close contact with the patient, none developed the disease.

The conclusion of most observers, that the period of infectivity is practically confined to the catarrhal stage, was borne out in this epidemic, although all cases were isolated for at least six weeks.

Treatment.—An accurate appreciation of the value of treatment in whooping-cough is admittedly impossible. Is the length of the whooping stage a satisfactory criterion? It varies from case to case apparently without rhyme or reason. However, like other observers in this field have done before us, we yield to the temptation to summarize results in a table, the limitations of which are self-evident.

TABLE III

Method of treatment	Number of cases treated	Average duration of whoop
Ephedrine	4	4.2 days.
Belladonna	9	6.6 "
Belladonna and vaccine	6	18.6 "
Ephedrine and vaccine	4	22.7 "
Belladonna and adrenalin	2	29 "

A word of explanation is necessary; ephedrine treatment consists of ephedrine hydrochloride (P. D. & Co.), gr. 1/2, three times a day for a child of 6 years, reducing the dose if sweating or flushing occurs; belladonna treatment consists of increasing doses of the tincture in a sedative expectorant mixture, until marked dilatation of the pupil occurs; vaccine treatment consists of hypodermic injections of 'Pertussis

Immunogen (Combined)', (P. D. & Co.), rising from 0.2 c.cm. to 0.8 c.cm. for a child of six years; and adrenalin treatment consists of adrenalin hydrochloride, minims iv, four times a day.

The superior efficacy of ephedrine in the above table is only apparent, as three of the four cases were the last three cases in the series. As regards the vaccine treatment, it is a curious, but perhaps not significant, fact that five out of the six relapse cases were treated with the vaccine.

It will be observed that no mention has been made of the well-known rectal ether medication. This was given a trial during the third relapse in a girl aged six. Ether was administered for a full week in the orthodox manner, but the whoop did not decrease at all.

In one case refractory to treatment, the Sister administered a stern rebuke, with immediate curative effect.

Summary of treatment.—The conclusion is unavoidable that none of the methods used in this epidemic appeared to stand the test of practical experience. Are the encouraging results reported by some observers, due to the character of the epidemic, and not to the treatment at all?

This question forced itself upon the writers when faced with the more baffling and refractory cases.

The skin reaction.—At the suggestion of Lieut.-Col. J. A. Sinton, V.C., I.M.S., the possibility of there being a skin reaction to determine susceptibility to whooping-cough, on the analogy of the Schick reaction, was investigated.

The antigen used was 0.02 c.cm. of 'Pertussis Immunogen' (P. D. & Co.) diluted to 0.2 c.cm. with normal saline. For the controls, a similar dosage of vaccine, after being heated to 75°C. for 10 minutes, was used. Preliminary trials pointed to this dosage as being suitable.

The children selected were girls between the ages of 14 and 17, of whom 26 had had whooping-cough ('theoretical immunes') and 33 had not ('theoretical susceptibles'). The following table shows the results obtained:—

TABLE IV

	Theoretical immunes	Theoretical susceptibles
Control and antigen reactions equal.	13 out of 26	12 out of 33
Control reaction exceeded the antigen.	9 out of 26	3 out of 33
Results analogous to 'Schick'	6 out of 26	9 out of 33

The table shows that, judging from the large percentage of anomalous results, there is no skin reaction in whooping-cough analogous to the Schick reaction in diphtheria.

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'NOVOSTIBUREA' IN THE TREATMENT OF KALA-AZAR

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and

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THE success of pentavalent organic compounds of antimony in the treatment of kala-azar has led investigators to search for new and more advantageous compounds in the field of organo-metalloid compounds. The well-known compounds—urea stibamine and aminostiburea—though they have many advantages over the simpler antimony salts—have still the disadvantages that they are fairly toxic and cannot be injected except through the vein, and that if they are used intramuscularly they produce bad after effects. Messrs. The Union Drug Co., Calcutta, in placing this drug at our disposal, claimed that it was practically non-toxic and could be safely used intramuscularly and even subcutaneously. The toxicity of this drug was found to be about 400 milligrammes per kilogramme weight of body, as compared with 225 milligrammes per kilogramme of urea stibamine and aminostiburea.

The compound is described by the manufacturers as the sodium salt of urea stibamine. It is prepared by dissolving urea stibamine in caustic soda solution, carefully neutralizing the excess caustic with acid, then saturating the solution with carbon dioxide, filtering, and finally precipitating with sodium chloride. The sodium salt is collected and dried on a porous plate in a vacuum over sulphuric acid. The compound is supplied in sealed ampoules labelled 'novostiburea'. The preparation is in the form of light yellow powder forming a clear yellowish solution. It can stand boiling. The manufacturers claim that even tap water may be used for making the solution and advise that in such cases the solution should be boiled before

(Continued from previous column)

A subsidiary series was taken, of five children, between 3 and 7 years, who had recently recovered from an attack. Four of these showed no reaction in either arm, i.e., were 'Schick-negative' to whooping-cough. The fifth, who had been a very mild case indeed, showed a mild reaction to the antigen only. Thus recent cases can be said to give 100 per cent consistent 'Schick' results.

This investigation, however, goes to prove that a skin reaction for whooping-cough is never likely to enter the sphere of practical politics.

We are indebted to the courtesy of the Principal of the School for permission to publish these notes, and to the children who volunteered for the skin tests.

TABLE

Serial number	Religion and sex	Ages	Duration of illness in months	Weight in pounds on admission	Number of injections prior to cessation of fever	Total number of injections given	Total quantity of the compounds injected in grammes	Frequency of administration	Gain or loss of weight on discharge	SIZE OF SPLEEN BELOW COSTAL MARGIN IN INCHES		LEUCOCYTE COUNT PER C.M.M.		REMARKS
										Before treatment	After treatment	Before treatment	After treatment	
1	H. M.	30	2	78	6	9	2.1	T.W.	++	6	5	4.1	5.0	Discharged cured.
2	M.M.	20	2	80	3	10	2.4	B.W.	++	6	5	2.5	4.4	Discharged cured.
3	H.M.	25	3	98	2	8	2.5	D.	++	3	3	4.4	5.6	Discharged cured.
4	H. F.	14	5	54	2	8	2.2	D.	++	8	8	2.5	3.1	Discharged cured.
5	H. F.	45	2	76	5	9	2.4	D.	++	4	3	3.1	5.6	Aldehyde and Chopra's test negative on discharge.
6	H.M.	16	1	84	3	8	2.1	D.	++	3	2	4.4	6.3	Discharged cured.
7	H. F.	12	10	50	3	11	2.1	T.W.	+	5	4	2.8	3.8	Discharged cured.
8	H. F.	12	5	58	8	11	2.1	T.W.	+	5	3	3.8	4.1	Aldehyde and Chopra's test negative on discharge.
9	H. M.	12	9	43	7	11	2.1	B.W.	±	6	4	2.3	3.6	Discharged cured.
10	H. F.	12	12	32	4	10	1.9	B.W.	±	5	3	2.1	4.0	Discharged cured.
11	H. F.	12	3	56	3	8	1.7	T.W.	±	6½	6	3.1	5.0	Discharged cured.
12	M.M.	6	2	28	3	7	0.9	D.	±	3	2	3.8	5.3	Discharged cured.
13	H. F.	3	4	18	3	11	1.1	B.W.	±	5	4	2.0	1.3	No effect.
14	H. F.	7	18	31	3	9	1.3	D.	±	4	4	3.1	3.8	Discharged cured.
15	H.M.	5	1	28	6	9	1.3	D.	±	3½	3	4.1	4.4	Discharged cured.
16	H.M.	7	1	23	4	9	1.4	D.	±	3½	3	3.1	3.8	Discharged cured.
17	H. F.	22	12	78	7	8	2.1	T.W.	±	8	8	3.8	4.4	Was treated before for kala-azar. Not much improvement.

B.W. = Bi-weekly.
T.W. = Tri-weekly.
D. = Daily.

use. For our use we prepared the solution either in tap water or distilled water, boiled in each case before use; this boiling rather improved the solution.

The conclusions, which we have arrived at, are the result of a study of 27 cases treated with this drug in the Public Health Department Kala-azar Centre. These patients were diagnosed as kala-azar by putting them under the following tests. On the first day of admission blood was taken for the total leucocyte count, differential count, search for malaria parasites, aldehyde test and Chopra's stiburea test. The patient was at the same time put under quinine in adequate doses for 3 days. If on the next attendance it was found that quinine had had no effect on the fever and all other tests indicated kala-azar, the patient was diagnosed as a case of kala-azar and the treatment commenced with novostiburea. Many of the patients come from distant villages sometimes 10 miles from Bandel and therefore had a tendency to become irregular in attendance as well as to stop treatment earlier than was desirable. This is the experience of all such kala-azar treatment centres existing in Bengal. As soon as the fever stops the patients, who are mostly poor cultivators, think that they have been cured and refrain from coming to the centre.

Out of the 27 cases, 20 were treated by the intravenous route and 7 were given intramuscular injections. Of the 20 cases treated by the intravenous route, 9 were given injections twice weekly, 7 injections thrice weekly and 4 injections daily, and of the 7 treated intramuscularly 3 were given twice weekly, one thrice weekly and 3 daily injections.

The table gives details of the results of treatment in all those cases in which the full course was completed.

From our experience the following conclusions have been arrived at:—

1. The compound can be safely given both by the intravenous and intramuscular routes.

2. The tissue does not become painful after intramuscular injection. Complaint of unusual uneasiness was not received even from cases coming from a distance of 10 or 12 miles.

3. The toxicity of the drug is so low that it can be given daily without any untoward symptoms.

4. There is a possibility of a daily injection of this drug effecting a much earlier cure.

5. In the 19 patients to whom the drug was given intravenously and was effective in stopping fever, the average number of injections required before the cessation of the fever was 3.6; in 4 it took two and in 10 only three injections. Whereas in the 7 cases by the

intramuscular route this average was 4.5 and the earliest cessation of fever was reported after three injections; this occurred in 3 patients.

6. In the 15 cases who had completed the course of treatment before they were discharged as cured, the average number of injections required was 9.

7. In the 4 adult cases who completed treatment the quantity of this compound required was an average of 2.35 grammes.

8. Marked gain in weight was noticed during the course of the treatment.

9. Marked improvement in the blood picture was also noticed.

10. In at least 4 cases at the end of the course of the treatment the aldehyde and Chopra's stiburea test had become negative; two of these had been given daily injections.

We wish to express our thanks to the Director of Public Health, Bengal, for kindly permitting the junior writer of this paper to work in the Bandel kala-azar centre to make these observations on the action of this drug on kala-azar patients and to Messrs. The Union Drug Co., Ltd., of Calcutta, for their generous supply of the drug with which the cases have been successfully treated.

(Note.—Novostiburea was used at the Calcutta School of Tropical Medicine as long ago as 1925 and the following reference to it will be found in the report of the School for that year. 'Only 4 cases in which Novostiburea was used can be included in this report.....; these were apparently cured with 10 injections given over a period of about 23 days'. Our experience in the following year was less satisfactory, as in the 20 cases in which this drug was used there were a number of relapses, but in the annual report for 1926 we commented on the low toxicity of the drug. Although the stability and the very low relative toxicity of this compound were strong recommendations, we did not feel that these compensated for its slower action and the lower degree of efficacy—compared with certain other antimonials which we were using at that time—that our first clinical trials indicated, and for this reason we did not extend our experience with Novostiburea.

However, this drug has enjoyed a certain degree of popularity on account of the special advantages we mention above, which it undoubtedly possesses, and we are pleased that it has been given a further clinical trial on scientific lines. Drs. Sur and Neogi's paper suggests that its degree of efficacy is very little, if any, less than that of urea stibamine and other antimonials now commonly in use, but, of course, they did not follow up their cases to see whether relapses occurred.—Editor, *I. M. G.*)

A Mirror of Hospital Practice

A CASE OF SPONTANEOUS PNEUMOTHORAX

By HUGH W. ACTON, C.I.E.

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and

DHARMENDRA, M.B., B.S.

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SPONTANEOUS pneumothorax apart from the type associated with active tuberculosis is generally believed to be very rare; this is not so, however, because many cases are missed. Weber (1919) found about two hundred cases of spontaneous pneumothorax in apparently normal persons reported up to 1919; after that date there have been frequent references to such cases in the literature, very recently Palmer and Taft (1931) have described six cases, and Kjaergaard (1932) gives full clinical histories of fifty-one cases. In our study of about one hundred and fifty asthma cases we have come across one case of spontaneous pneumothorax simulating very closely a case of asthma. This case is reported with a short note on the aetiology of the condition with a view to bringing out the importance of this lesion.

Spontaneous pneumothorax is a term used for every case of pneumothorax which is not artificial or traumatic, i.e., where the presence of air in the pleural cavity is from any internal cause. Some authors consider as spontaneous only those cases in which there is no associated pathologic change in the lung, i.e., idiopathic spontaneous pneumothorax. Amongst cases of spontaneous pneumothorax in which there is an associated pathological change in the lung, 80 to 90 per cent are in tuberculous patients and are due to a tuberculous process, usually a cavity or caseation of a tuberculous gland and contiguous lung tissue. It is usually accompanied by a fluid pleural effusion and the prognosis is very grave; the patient generally does not recover, but there are rare examples of rapid recovery from pneumothorax unaccompanied by pleural effusion. Cases of spontaneous pneumothorax have been described in broncho-pneumonia and influenzal pneumonia. The idiopathic spontaneous pneumothorax, as the name implies, occurs in apparently healthy people and as a rule is not accompanied by any pleural effusion although some cases with effusion have been described. The prognosis in this type is very hopeful, they improve very rapidly and the average period of recovery is about five to ten weeks; no special treatment is required.

The condition is due to rupture of scar tissue caused by adhesions between visceral and parietal pleura, or of an emphysematous bulla

on the margin of the lung. The scar may be due to a small old healed tuberculous focus or to some other previous inflammatory process. The emphysematous bulla may similarly be the result of a tuberculous scar or secondary to some other condition. Some authors are of the opinion that all cases of idiopathic pneumothorax are tuberculous in origin, the tuberculous infection not being accompanied by any physical signs or positive radiological evidence. A theory has also been advanced (Palmer and Taft, 1931) that there is a tuberculous focus present causing the rupture; the collapse of the lung following the rupture and the resulting rest allow it to heal entirely without leaving any scar. Other workers believe the cause of these idiopathic cases to be non-tuberculous always.

Weber (1919, 1921 and 1932) maintains that the cause is mostly the rupture of a minute superficial emphysematous bulla (just below the visceral pleura) adherent to the parietal pleura—resulting from a healed miliary tubercle. As a result of local tuberculous lesions—for instance, a subpleural tubercle—there might be a local scar fixing a point of the lung to the parietal pleura. Close to such a scar there may be an emphysema bleb and the rupture of such a bleb might be due to some sudden movement accompanied by some sudden respiratory effort. The only difference, according to him, between the idiopathic spontaneous and the tuberculous spontaneous cases is that the idiopathic cases are connected with healed, non-virulent sterile lesions whereas the tuberculous cases are connected with still more-or-less-virulent foci containing living bacilli. On the other hand most of the cases of idiopathic pneumothorax reported have been in previously healthy people with no demonstrable pathologic change in the lung and the subsequent history showed them to be in normal health. Recently Oliver and Taft (1931) have reported six cases, in five of which the subsequent history was followed. Kjaergaard (1932) re-examined forty-nine cases three or more years after the pneumothorax and in forty-eight he could find no clinical or radiological evidence of tuberculosis, in the remaining one the patient was quite well for three years after right spontaneous pneumothorax and then developed acute tuberculosis of the left lung. Kjaergaard emphasizes that the spontaneous pneumothorax occurring in otherwise healthy individuals is not a manifestation of pulmonary tuberculosis. He thinks that the condition is due to the rupture of a valve vesicle, of which he describes two types—namely scar tissue vesicle and emphysematous valve vesicle.

Description of the case.—A European male, aged thirty-three years, was admitted into the hospital suffering from dyspnoea and orthopnoea on 2nd May, 1932, to be investigated for asthma. The trouble was of three weeks' duration, the dyspnoea started suddenly one evening when he was resting after his day's work.

All of a sudden he felt a choking sensation in his chest, the acuteness of the condition lasted for a few hours only. Since that day until the time of admission he had been suffering from dyspnoea, orthopnoea and cough; difficulty in breathing was most marked from 8 A.M. (when he got up from bed) to about 11 A.M., and it came on in spasms, each spasm lasting for about fifteen minutes.

Family history.—There was no family history of asthma; urticaria, eczema, or other allergic condition.

Personal history.—He had never previously suffered

Treatment.—No treatment other than rest in bed for a short period was advised. The patient improved rapidly and has been free from symptoms from that time. A skiagram taken on 5th September, 1932, i.e., four months and two days later (see figure 2) showed that the right lung had expanded fully, the right pleura was thickened and there were numerous small calcareous areas scattered near the bronchioles; there was a very doubtful peri-hilar lesion. Numerous small calcareous masses were present on the left side but there was no evidence of consolidation.



Fig. 1.—Skiagram of the chest showing complete collapse of the right lung.



Fig. 2.—Skiagram taken four months later showing the right lung fully expanded.

from asthma, urticaria, or eczema. Six years ago he suffered from pleurisy and since then had been suffering from bronchitis.

Physical examination of the chest.—The right base was dull, and on the right side, breath sounds were very feeble and the coin sound was present. There was slight myotatic irritability. The apex beat was in its normal position.

A skiagram taken on 3rd May, 1932, showed complete collapse of the right lung (see figure 1).

Blood count.—

Total leucocytes ..	9,000
Total eosinophiles ..	270 (3 per cent).
Hyalines ..	5 per cent.
Mononuclears ..	20 "
Polymorphonuclears ..	72 "
Arneth's count	I II III IV V
	19 40 35 4 2

Sputum.—Numerous pus cells, no eosinophiles. No acid-fast bacilli. Pneumococci and *Micrococcus catarrhalis* present.

Stools.—Trichuris ova. No *Entamoeba histolytica* and no pathogenic bacteria.

Urine.—Specific gravity 1016. Reaction acid. No albumin or sugar. Ether test for proteoses—positive.

Dermal tests.—Negative to hairs, feathers and various foods.

Von Pirquet test.—Positive.

Basal metabolism rate was ascertained to find out how far the left lung had taken up the function of the collapsed lung; oxygen consumption was 26 per cent below normal.

Features of the case

- (1) The onset of the trouble was not associated with any exertion.
- (2) There was no pain at the time of onset.
- (3) The dyspnoea and the orthopnoea were not continuous, but came on in spasms thus simulating very closely a case of asthma.
- (4) The position of the heart was unchanged.
- (5) The recovery was rapid and no special treatment was required.
- (6) Considering the previous history of pleurisy, the positive von Pirquet test and x-ray picture taken after the lung had expanded the pneumothorax in this case is very likely to be due to the rupture of a superficial emphysematous bulla resulting from a healed tuberculous focus.

REFERENCES

Kjaergaard, H. (1932). 'Spontaneous pneumothorax in the apparently healthy.' Reviewed in *Brit. Med. Journ.*, 1932, Vol. I, p. 712.
 Palmer, J. P., and Taft, R. B. (1931). *Journ. Amer. Med. Assoc.*, Vol. XCVI, p. 653.
 Weber, F. P. (1919). *Practitioner*, Vol. CII, p. 190.
 Weber, F. P. (1921). *Lancet*, Vol. II, p. 940.
 Weber, F. P. (1932). *Brit. Med. Journ.*, Vol. II, p. 889.

A CASE OF IMPACTED VESICAL CALCULUS

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and

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H. G., a Muslim, aged 40, was admitted to the Civil Hospital, Parachinar, on the afternoon of 14th December, 1932, complaining of retention of urine.

The history was that for some months previously he had had some frequency of micturition with pain at the point of the penis on conclusion of the act; that latterly there had been some involuntary dribbling of urine; and that twenty-four hours before admission sudden and complete retention of urine had supervened.

On palpation of the abdomen it was found that the bladder was full and distended to a level three inches below the umbilicus in the middle line.

On the presumption that such a sudden onset of retention of urine in a man of his age was due to urethral spasm or congestion, the patient was put under an anæsthetic (A.C.E. mixture) and an effort was made to affect relief by means of a soft rubber catheter. But it was found impossible to pass this into the bladder and a metal one was next tried. This however also failed and a definite hard and unyielding obstruction to its passage was made out high up in the posterior urethra.

In view of the history of frequency, and pain at the end of micturition and the obvious possibility of the retention being due to a stone, the attempt was not pressed any further. As a measure of temporary relief the bladder was aspirated suprapubically and the patient prepared for operation on the following morning.

A suprapubic cystotomy was performed through a median vertical incision. As soon as the aperture in the bladder was large enough to admit a finger a stone was found which was firmly fixed in the prostatic urethra completely blocking the entrance from the bladder. It required considerable force to dislodge it.

On delivery it was found to be a small uric acid stone roughly pear-shaped in outline, flattened antero-posteriorly and showing a definite constriction or neck broadening out to a head beyond.

Looking back on the symptoms displayed one could now explain the frequency of, and pain on, micturition, as being due to the calculus acting as a foreign body in the bladder; this was followed by incontinence which presumably was due to the stone interfering with the action of the sphincter, after its impaction; and, later still, the sudden retention which was probably determined by a local chill or congestion. There can be little doubt that had this acute complication not supervened the stone would have gone on growing, partly in the bladder and partly in the urethra, and would ultimately have developed into a true 'hour-glass' calculus.

The patient made an uninterrupted recovery and was discharged from the hospital on the seventh day after operation.

PROLAPSE OF LUNG FOLLOWING AN INJURY

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ON 29th October, 1932, Bahawal, a Moham-madan male, aged 35 years, was brought to the dispensary with the following injuries:—

(1) An incised wound 5 inches by 1½ inches on the right side of the chest in the mammary region; the third, fourth, fifth and sixth ribs were severed and a large portion of the right lung was prolapsed through the wound.

(2) An incised wound 3 inches long just above the left wrist, both bones of the forearm were completely cut, the hand was only hanging by the skin and flexor tendons.

Besides the above injuries he had others as well. At the time of admission he was in a moribund condition with severe symptoms of shock, but he was conscious. The injuries had occurred about twelve hours previously and the parts were wrapped in dirty rags.

Treatment.—Under chloroform, the prolapsed lung was washed with normal saline and was replaced in the chest. The pleural cavity was cleared of blood clots. Bleeding points in the chest wall were secured and the wound was stitched in layers without any drainage. His left forearm wound was cleaned thoroughly with water and saline lotions, and dabbled with acriflavine lotion 1—1,500. The bones were approximated and the wound was stitched without drainage and the arm was fixed in an antero-posterior splint. All his remaining injuries were similarly treated and were stitched.

All the wounds united by first intention. On the seventh day all stitches were removed, the left side of the chest was strapped as some of the ribs were fractured.

During all this time he complained of pain in the left side of chest and was running a temperature; gradually he developed signs of effusion on this side. On 17th November his chest was explored and fluid was detected. On 23rd November one pint of blood-stained fluid was removed from the left side of his chest, the first portion of the fluid containing some pus. The immediate effect of this operation was good and he became comfortable. Signs of pleural effusion did not disappear and on 27th November another exploration of the chest was done and pus was detected in the pleural cavity.

As the patient felt easier he refused an open operation for his empyema and on account of the nature of the exudate a subsequent aspiration was not successful. On 2nd December he started expectorating pus, and in about ten days he was quite free of all signs of effusion and his temperature became normal.

Splints from the arm were removed after the usual time and he had a firm union.

Two months after admission he was discharged cured on 19th December, 1932, and since then he has been keeping in perfect health.

I am greatly obliged to Sardar Sahib Dr. Hira Singh, my Civil Surgeon, for permission to publish this case and for his advice.

AMMONIUM CHLORIDE IN THE TREATMENT OF NEPHRITIC ŒDEMA

By S. K. ROY, M.B.

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A MAN, aged 26, suffering from ascites and marked generalized œdema of eight months' duration, came to hospital for treatment.

He was passing a greatly diminished quantity of urine which contained much albumen.

He was put on the following mixture three times a day:—

Ammonii chloridi	..	grs. 30.
Extracti glycyrrhizæ liquidi	..	min. 30.
Aquam menthæ piperitæ	..	ad ʒi.

Later, the dose of ammonium chloride was increased to grs. 40 and it was continued without any untoward symptoms.

In addition compound jalap powder—grs. 30 to grs. 60—was given bi-weekly according to the degree of constipation.

A salt-free diet of milk, rice and fish 4 ounces per day was given and the amount of fluid was restricted.

There was marked diuresis and in about four weeks' time complete disappearance of ascites and œdema except a little puffiness of the dorsum of both feet.

Indian Medical Gazette

MAY

AIR TRAFFIC AND YELLOW FEVER

For every step we make along the road of progress payment in one form or another is exacted from us. Hitherto the cost of air transport has been slight in proportion to the gain, but unless we are on our guard and, from time to time, frame new international quarantine regulations to keep pace with the altered conditions, the loss that is possible to the world from the introduction of air-craft far outweighs the profit.

The speed of intercommunication between countries distant from one another has had the effect of bringing them near together. Formerly all the major infectious diseases were more or less limited to certain places because, with only a few exceptions, the time taken in ocean travel from endemic centres to other countries was greater than the maximum incubation periods of these diseases, so that any cases which might occur on board were discovered before the ship could reach the port of another country. But now, with journeys that used to take weeks reduced to a few days, it is possible for infected, though apparently healthy, persons to journey between almost any two countries in the world during the incubation period of any of the important infectious diseases. India as the principal home of plague and cholera is no doubt being carefully watched by the rest of the world, and we in turn have our eyes fixed on the endemic centres of yellow fever, which is our greatest menace.

The two centres of yellow fever in the world are Central America and the West Indies with the northern part of South America, and an extensive area of West Africa embracing all the British, French and possibly Belgian possessions there. At present the American focus is of no importance to India, but West Africa most certainly is. The mosquito vectors of yellow fever already exist in large numbers in East Africa, Egypt, India and the rest of southern Asia, all the islands of the East Indian archipelago and Australia. Therefore if once yellow fever breaks its bounds and reaches the western shores of the Indian ocean it will almost certainly continue its destructive course throughout tropical and subtropical Asia and the numerous islands to the south.

It has been argued that because this disease has never spread from the west to the east side of tropical Africa there is some unknown factor preventing this. What little evidence we have is quite against this theory for there is no evidence of racial immunity to infection

with yellow fever except such as is acquired by the races long resident or aboriginal in countries where it is endemic, and also it has been shown that mosquitoes taken from India to England act as efficient transmitters of the virus in the laboratory. The most probable explanation of the restriction of yellow fever to one side of the African continent for many centuries is that hitherto communication across central Africa has been infrequent and slow, and in the centre there is high land with a relatively cold dry climate which is probably unsuitable for the development of the virus in the mosquito. There has thus probably been a permanent break in the chain whereby infected persons and mosquitoes might have been expected to have gradually carried the disease from village to village from west to east. But now with air transport almost daily opening up new communications throughout Africa, it will not be long before it will be possible to cross the continent in two or three days at the outside and thus bring infected mosquitoes, as well as men in a stage capable of infecting mosquitoes but showing no signs of illness, to countries hitherto free from yellow fever. From Mombasa to India *via* Aden would only take three or four more days so that it may soon be possible for a man to reach India from West Africa in about a week. It is now authoritatively in some quarters stated that a person is infectious to mosquitoes for the whole incubation period which may be as much as ten days, as well as being infectious during the first three days of the attack. It is therefore clear that once air travel between West Africa and India becomes an accomplished fact it will be possible for an apparently healthy man who is infective to mosquitoes to reach India. The terrible implication of this is so clear that it needs no emphasis.

Should such a person reach India and infect some of the local mosquitoes the disease would almost certainly spread throughout the country with extreme rapidity and no sanitary or quarantine measures would be of any avail to check it. The reason for this strong expression of opinion is based on the analogy of dengue fever which shows similarities to yellow fever in many respects, as well as being transmitted by the same species of mosquito. We have numerous instances in the history of dengue of a sudden outbreak spreading throughout a wide area in a very short time and infecting almost all the population; the most recent example of this was the outbreak in Greece a few years ago. India is on the direct route to the rest of the East and should yellow fever reach here it would almost certainly spread to all the other countries where members of the genus *Aedes* are found, and which have been enumerated above. This makes it clear that in keeping yellow fever at bay we will be saving millions of people in other countries further east as well as in India itself.

It is true that H. R. Carter, than whom no one has had wider experience of yellow fever in America, is of the opinion that the spread of yellow fever is very limited as the infective mosquitoes are typical house dwellers and do not travel far from their original breeding places (the maximum he gives is 100 metres). We do not combat the accuracy of this observation, but no such limitation is observable in the spread of dengue fever during an epidemic, therefore we consider it justifiable to guard against yellow fever on the assumption that it will spread with a rapidity equal to that of dengue if it were to gain entrance to a country where such widespread explosive epidemics have been experienced on more than one occasion.

Another opinion held by some is that an attack of dengue will protect against a subsequent attack of yellow fever. Protection experiments with serum of persons recently recovered from dengue have so far failed to show any evidence of this.

The advisers on public health matters to the Government of India have long been wide awake to the dangers outlined above and in our correspondence columns in June 1929 the present Director-General of the Indian Medical Service, at that time Surgeon-General with the Government of Madras, published a letter in which he drew attention to the salient facts and counselled error on the side of safety regarding the prevention of the entry of yellow fever by aeroplane into India. We also have evidence that a year or so earlier than the publication of his letter this important matter had already attracted his attention.

Since that time he and his associates at headquarters have been untiring in their efforts to have world regulations of a east-iron nature framed to protect India from any possible chance of acquiring yellow fever. The aerial convention of the Office International d'Hygiene Publique adopted certain articles in which they placed the responsibility of guarding against the transmission of yellow fever by aeroplane from endemic centres on the country of origin, giving powers of veto of entry to the countries to which the aeroplanes might travel only on condition they provided an adequate explanation of such action. This was unsuccessfully combated by the Government of India through its public health advisers. But in May last year the efforts of the Director-General were slightly more successful, for as the result of an address delivered before the Yellow Fever Commission of the Office International d'Hygiene Publique after the articles of the convention had been decided upon, it was agreed that countries which considered themselves threatened with yellow fever should be the judges as to whether air traffic from infected or suspected countries should be prohibited.

On account of this we in India are looked upon as alarmists. This is made clear by the

following paragraph translated from the report of the Commission on Yellow Fever of the Office International, which is published in their monthly Bulletin of January last:

'It can be said that the chapter on yellow fever of the International Sanitary Convention for aerial navigation is a concession to the alarmist point of view. As it is the Yellow Fever Commission of the Office International d'Hygiene Publique which bears the responsibility of having enunciated the principles on which this code of rules is based, we have no hesitation in saying that except by totally forbidding aerial navigation we could not prescribe more rigid plans. The hygienists who for the last twenty years have borne the task of preventing the spread of yellow fever, which raged in Panama and other ports, have said that these proposals have exceeded the necessary limits'.

This may be so, but in these places yellow fever has already occurred and they are in close touch with countries in which the disease is endemic, so there is possibly a certain amount of acquired protection among the inhabitants which assists in keeping it at bay. Such conditions are entirely absent from India.

A great deal of work is now being done on yellow fever and important advances have been made recently. One of the most important of these from our point of view is the preparation of a fixed virus in the brain of a mouse which when inoculated along with the serum of a recovered yellow fever patient confers a considerable degree of immunity. If this immunity is eventually shown to be certain of production the compulsory vaccination of all travellers by aeroplane from an infected or suspected yellow-fever country to a yellow-fever-free country would greatly simplify the precautions at present necessary.

As a consequence of the importance of this matter to which the public health advisers of the Government of India have been largely instrumental in attracting the attention of other prominent sanitarians, a conference was held at the end of last year in South Africa. The Government of India was represented and no doubt their point of view was kept alive. Leading laboratory workers also attended so that the latest discoveries regarding protective vaccination and the mapping of yellow fever endemic centres by special animal experiments could be fully explained. The report of this conference is not yet received but it will no doubt be of great value and interest when it finally appears. But whatever the findings of the conference and whatever the weight of authority behind it, if it recommends the relaxation of the present regulations in any way, unless these recommendations are based on fully-proved facts and not on opinion, however experienced, we feel that the Government of India

will be justified in maintaining its present uncompromising attitude. Our reason for supporting this attitude of maintaining absolute certainty in the exclusion of yellow fever from India may be explained by a hypothetical example.

On the entirely imaginary assumption that India felt she must even go to war to keep out yellow fever, the cost of such a campaign would almost certainly be less than the cost of introduction of yellow fever to India and the countries further east.

Medical News

MEDICO-LEGAL AND CRIMINOLOGICAL REVIEW

If we may judge from the comparative neglect of the study of forensic medicine in England, as distinct from Scotland, the insatiable appetite of the public for information on the problem of crime is apparently not shared by medical men in their professional capacity. To meet the public taste popular articles on crime questions, modern methods of analysis, etc., are now a commonplace of the lay press. Scientific papers on these subjects by authoritative writers are, however, infrequent, and the medical enquirer must to a large extent confine his reading to textbooks. There are several reasons for this, but one of them is certainly the absence of a suitable medium of publication. We have just received the first number of the *Medico-Legal and Criminological Review*, a journal which incorporates the Transactions of the Medico-Legal Society. It has been something of a reproach to English forensic medicine that there has been no journal to set against the excellent publications to be found on the continent of Europe, more particularly in Italy, and we congratulate the Medico-Legal Society on having taken a distinct step forward in publishing their transactions in journal form; this should have the effect of arousing interest in medico-legal problems among medical men generally. The first step in impressing the conservative legal mind with the possibilities of new methods of analysis, e.g., the application of blood-grouping tests to the solution of questions of paternity, consists in the formation of an organized body of medical opinion, which will be stimulated by the publication of a journal under the aegis of the Medico-Legal Society. There has hitherto been an impression that forensic medical science is a matter for Crown experts and largely deals with the dead. A new branch of medico-legal work is now rapidly developing which deals exclusively with the living. We refer to the increasing importance of medical examinations both for injuries and for diseases resulting from modern industrial conditions, which form the basis of legal actions of many kinds. This form of medico-legal work touches general medical practice very closely. We congratulate the Society on having secured Messrs. Baillière, Tindall and Cox as their publishers and we wish the venture every success.

Congress of any paper submitted by a member who is unable to attend.

Further information may be obtained from the local provincial secretaries or from the local secretary for the Government of India, Malaria Survey of India, Kasauli, Punjab, British India, or the Honorary General Secretary, Far Eastern Association of Tropical Medicine, Batavia-Centrum, Java.

FIFTY YEARS AGO

(From the *Indian Medical Gazette*, May 1883)

I would now venture to make these cases (of malarial cachexia) a peg to hang some observations on, regarding an affinity, fancied or real, which on the surface seems to exist between acute rheumatism and the malarial fevers. They alike originate in chills and damp, insufficient food and clothing. Their symptoms closely approximate, save in the presence of inflammation of the joints in rheumatism, but in famine or relapsing fever, which I believe to be a hybrid malarial fever, this too may not be wanting. There are the same high temperatures, sometimes reaching 107° in the height of a quotidian paroxysm, in Assam, and the same profuse sweats, and urinary sediments. Their ultimate morbid changes are not dissimilar. The plastic effusions of rheumatism are akin to the albuminoid degenerations of the malarial cachexy. In the one case the blood retains its vitality in all its component parts, in the other its red blood corpuscles and albumen suffer serious damage, resulting in the visceral and glandular hypertrophies so well known in this dyscrasy. Therapeutically they are influenced by the same remedies, viz, quinine, salicine, and the salicylates.

One grave objection to this view is the comparative infrequency of rheumatic fever in India. In an experience extending over thirty years, I have met with only one case of rheumatic fever, and I imagine most medical men in this country could count their cases of this disease on their fingers' ends. What can be the reason of this comparative rarity? Can the two dyscrasias be the same, and does the one disease supplant the other under the modifying influences of climate and local conditions, producing paroxysmal fever in the feeble, ill-fed and ill-clad races of India with its extremes of temperature and moisture instead of developing into the more sthenic disease?

Current Topics

Notice.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE, 9TH CONGRESS

THE Honorary General Secretary of the Far Eastern Association of Tropical Medicine announces that it has been decided that the 9th Congress which was to have been held at Nanking, China, from the 2nd to 8th October, 1933, will not be held this year. Notice of the dates and place of the next Congress will be intimated later.—EDITOR.

The Treatment of Conjunctivitis

By W. C. MACFETRIDGE, M.D.

(Abstracted from the *Medical Press*, 21st December, 1932, p. 509)

IN considering the treatment of conjunctivitis, it is first of all essential to bear in mind that the great majority of cases are due to bacterial infection. A few cases arise from other causes, such as smoke, irritant vapours, or errors of refraction, but the most common origin is microbic. As a rule it is not possible to say from a study of the clinical features of a case what the causal bacteria are, for a particular microbe does

not produce the same clinical appearances in every patient; and if we want to identify the micro-organism we must call in the aid of a bacteriologist. However, from the point of view of treatment it is generally not of great importance to be able to say what the exact microbe is. But patients must be warned against the danger of infecting others. They must be told that the discharge from the eyes is infective, and that towels, handkerchiefs, and other such articles are a common way of disseminating the disease. The conjunctiva is a membrane, and it forms in the orbit a mucous sac. When it becomes inflamed pus and muco-pus are secreted, and collect particularly in the folds and fornices of the conjunctiva. Our aim is to clear away all this purulent or muco-purulent discharge, and to destroy the invading microbes. It is a great mistake to put a bandage of any kind on a case of conjunctivitis. A bandage keeps the discharge in instead of helping to get it out; and by keeping the tissues bathed in pus it may easily produce serious damage to the cornea, which would be a very grave complication. It is not necessary to protect the eye from exposure to air. Fresh air is good for conjunctivitis, and patients should be encouraged to go out of doors. Let us now consider some of the principal means of treatment. Lavage of the conjunctiva is useful, and is essential in every case where there is much discharge. It washes out the pus and microbes and offensive material of all kinds, and cleans the conjunctival sac. The best way to carry out lavage is with a pear-shaped glass vessel called an *undine*, but if this is not available, it can be done very well with a glass funnel or the barrel of a large ear syringe, with a piece of rubber tubing attached. Whatever apparatus is used, it must be something that can be boiled *in toto*. Any bland lotion or weak antiseptic can be used, such as boric lotion, hydrarg. perchlor., 1 in 5,000, or Condy's fluid, 1 in 2,000, and the tepid lotion is directed in a gentle stream all over the eye and conjunctival sac, while the patient is instructed to rotate his eye in different directions so as to irrigate the various recesses as thoroughly as possible. This lavage is carried out two or three times a day, or, if there is much purulent discharge, as often as every hour.

Drops, or collyria, are an essential part of treatment. The most useful are zinc sulphate, argyrol, protargol, and silver nitrate. They are made up in watery solutions, and are best prescribed in half-ounce quantities. One drop of the solution is dropped into the eye three times a day, or oftener, with a glass dropper that must never touch the eye, and must be rinsed in boiling water before and after use. It is a good plan to put in the drops at meal time, as this regularizes the treatment. A drop should never be put in at bedtime, for the resultant reaction may interfere with sleep, and increased secretion may be pent up inside the closed lids. If one kind of drop does not seem to suit a case we should not hesitate to try another. Some drops lose their efficacy after a time; the conjunctiva seems to have got accustomed to them; while other drops, such as argyrol, produce an irritation if used too long.

Zinc Sulphate is one of the most useful of all eye-drops. It has the great merit of being clean and cheap, and is a specific in one kind of conjunctivitis—the angular variety. But it is rather pungent, and nervous patients complain that it is painful, and will not use it for this reason. The usual strength is two grains to one ounce distilled water, but we may begin with a weaker solution, and, if this is tolerated, work up to stronger solutions, as much as 1 per cent. A little boric acid is generally added.

Argyrol is a mild antiseptic collyrium, astringent, and not painful. Usually it is prescribed in from 10 to 30 per cent. solution, 25 per cent. being a good working strength. Like the other silver salts, it is supposed to have great penetrative power, but some authorities say that as a germicide it is negligible. Clinically it is beyond all doubt beneficial in many kinds of conjunctivitis, and as it is rather soothing, it often becomes a

favourite drop with patients. But it is messy, gives to linen a temporary brown staining, and if used over a long period may produce argyria. No patient should be allowed to use it unless under frequent observation. A patient of mine for whom I had prescribed the usual 25 per cent. argyrol drops disappeared for three months, and used the drops diligently in the interval; he then returned with an intractable brown staining of his conjunctiva, and said his appearance was spoiled.

Protargol is usually prescribed 2 to 5 per cent. Its uses are very similar to argyrol. It is of a light-brown colour, and is less likely to produce argyria, but it may give pain. On the whole, it is not so generally applicable and useful as argyrol.

Silver Nitrate is the most active and powerful germicide we have. It is greatly used in 2 per cent. solution, to be applied to the conjunctiva of the everted lids in gonococcal cases, in trachoma, and in other severe forms of conjunctivitis. Sometimes it is prescribed as drops in $\frac{1}{2}$ per cent. solution, but these should rarely be entrusted to patients as there is always danger of argyria.

Tannic Acid, grains 5 to the ounce, is useful, and a mild astringent collyrium.

We will now consider briefly some of the most common kinds of conjunctivitis:

Gonorrhoeal Ophthalmia.—In infants this is called ophthalmia neonatorum, and is a common cause of blindness. It is a most serious condition, alike in infant and adult, and the gravest view of the case must be taken from the start. It is not uncommon, if the gravity of the disease is not appreciated, to see both eyes lost within a few weeks. The most expert knowledge and treatment are necessary. As soon as the case is seen, active and vigorous treatment must be put in hand. Lavage with weak Condy's fluid, 1 in 4,000, every hour, or at any rate every two hours, is indicated. All pus must be cleaned away, and the eyes kept as clean as possible. Silver nitrate in 2 per cent. solution must be applied every morning to the everted lids, and $\frac{1}{2}$ per cent. drops instilled three times a day. The great danger is infection of the cornea, followed by ulceration and possible destruction of the eye.

Trachoma.—This is a very serious and very chronic form of conjunctivitis. Even in the most experienced hands, and with every opportunity for treatment, the average duration of a case is from four to five years. In patients who do not attend regularly the disease is practically incurable. The main treatment consists in the application to the everted lids of 2 per cent. silver nitrate in the early stages, and of copper sulphate stick in the later stages. This is done three times a week. The many complications that may arise, e.g., pannus, corneal ulcer, trichiasis, require special treatment. Patients should be warned as to the infectiousness of the disease.

Phlyctenular Conjunctivitis.—This is a disease of childhood and youth, and is the most common eye disease of children. It is thought to take its origin in the strumous diathesis, and undoubtedly is usually found in debilitated children. Treatment consists in application to the eye of unguentum hydrargyri oxid. flavi, 1 per cent., or of calomel powder once or twice a day; usually once is sufficient. The calomel is less irritating than the ointment, and may suit better in the early stages of the disease. If the cornea is involved, atropine must be added to the treatment. The general condition of the patient is very important. Fresh air and suitable food must be ordered. Cod-liver oil is very useful, varied perhaps with syrupus ferri iodidi. The disease is very liable to relapses, and treatment should be continued for some time after apparent recovery.

Angular Conjunctivitis.—This type of conjunctivitis is frequently met both in the acute and the chronic form. It is particularly common in a mild chronic form, with a little white discharge at the angles of the eyes. The specific treatment is zinc sulphate drops, from $\frac{1}{2}$ to 1 per cent. three times a day. If this is

carried out, cure is practically certain. The silver salts are of little use in this condition.

Acute Catarrhal Conjunctivitis.—This, a mucopurulent form of conjunctivitis, is of varying severity, and is often due to the pneumococcus. Treatment consists in the employment of the silver preparations, such as argyrol, 25 per cent., three times a day during the acute stages, and when the inflammation is subsiding we may change to the astringent drops, preferably to zinc sulphate. If in this form of conjunctivitis, or in any other form, the lids are stuck together at night by discharge, it is well to order a simple ointment to be smeared on the edges of the lids at bedtime. Boric ointment does very well for this purpose; unguentum hydrargyri oxidi flavi is too irritating, but a very useful and agreeable ointment is hydrargyri perchloridum, one part to three thousand parts white vaseline.

The Treatment of Diabetes in Children

By LOUIS R. GROTE

(From the *Prescriber*, Vol. XXVI, December, 1932, p. 349)

It is important that the practitioner should be familiar with the problem of child diabetes, as this disease is undoubtedly on the increase. The life-lengthening effect of insulin necessarily leads to an augmentation of the number of patients, and this naturally holds good with the younger generation. While in the pre-insulin era a diabetic child rarely lived longer than two years, experienced specialists now know a considerable number of young folk whose diabetes has had an existence of eight or ten years. I have a great many observations in which the diabetes has existed for more than eight years under constant protection of insulin, and in which a dangerous return of the disease is not to be expected. Without official registration an exact numerical statement is impossible, but approximate calculations induce me to believe that of every hundred diabetic persons from five to seven show the beginning of the disease before the sixteenth year. No fundamental difference exists between the disturbance of metabolism in childhood and that in adult life, but the symptoms of the former are in so many ways characteristic that a minute knowledge of details is necessary to carry out successful treatment. In earlier years child diabetes was usually regarded as a severe case, which was justified in consideration of the hopeless prognosis. In accordance with this fact, to-day we can state that about 90 per cent. of all diabetic children need insulin and usually continue to need it. But it is necessary to add that I cannot believe altogether in the dogmatic certainty of this somewhat dismal prognosis of the future. Observation of children, who have been diabetic for five years or longer, leads me to believe that with them also an increase of tolerance is possible and that the development into a diabetes absolutus (that is, a constant, unrepairable disturbance of the pancreatic activity) is by no means inevitable. In about ten years we shall be able to judge these questions better than to-day.

The exact observation of each single case shows greater variety within the range of the general need of insulin. It is very natural to regard the quantity of insulin required as a measure of the seriousness of the case, but by this schematic method we cannot accurately judge the different situation of the individual patient. The amount of insulin required is a factor to be determined mainly by the quantity of carbohydrates to be assimilated, and by the mass of cells of the body to be supplied. In the absence of an exact method for the determination of the insulin produced by the organism itself, the exact quantity of the insulin of a normal person is as yet not available. It is most probable that this production is mainly dependent on the two factors equally. I have suggested that the degree of serious-

ness of a case of diabetes may be measured by forming a product of the quotients—quantity of insulin (units): body-weight (kg.), and quantity of insulin: carbohydrates of the food (gm.), which as compensatory index approximately indicates the degree of the sickness. For simplification we multiply the result by 100. This index is reckoned on absolute aglycosuria and an optimal food supply corresponding with the state of growth of the child. I have watched this index during the last few years in many children, and I have found that in a surprisingly high percentage it improved. When the index lowers to 0, the child lives without insulin. Experience shows that an index above 100 corresponds to a relatively dangerous phase of the disease, in which dropping of insulin even for a very short time must lead to heavy acidosis or coma. It was noted, however, that children whose index in a certain state was far above 100 nevertheless were able to improve their tolerance by consequent use of insulin, and they again reach a phase of their metabolic disturbance far less dangerous than before.

The difficulties of the treatment of the child lie mainly in the greater lability of the blood-sugar regulation as compared with the adult. While in the adult a certain dose of insulin causes a gradual descent of the blood-sugar during the next three or four hours, which, if the dose is not extreme, does not overstep an amplitude of 100 mg. per cent., the same dose with a child under equal outward conditions (food) brings the blood-sugar down from 350 to 100 or even 50 mg. per cent. within a far shorter period. Therefore hypoglycæmic shocks are far more frequent in children than in adults. They develop faster and lead to stronger nervous indispositions, unconsciousness, cramps, and paralysations. But as hyperglycæmia can follow this state within a very short time, we often find in our practice that the physician cannot explain this paradox of a combination of great quantities of sugar in the urine and nearly simultaneous clinical hypoglycæmia as the result of incompatibility with insulin or resistance on the part of the child. It is important to point out this frequent mistake. Real resistance against insulin is very rare, and in childhood I have not seen it during my long experience. The combination mentioned leads to the fundamentally important fact in the treatment with insulin of a child, namely the necessity not only to define the injection in quantity, but also to adapt it in time to the curve of blood-sugar. Most children reach the highest point of their blood-sugar in the early morning hours between 5 and 7 o'clock. A second rise between 4 and 6 in the afternoon corresponds to this height. But there are many exceptions. The task of the clinical observer is firstly to control the blood-sugar every hour or second hour. The distribution has then to be done in such a way that the insulin is given on the ascending curve. This way alone prevents hypoglycæmia. Such outbreaks can discredit the whole insulin therapy.

The factors ruling the movement of the blood-sugar are manifold. From outside influence the food supply is of main importance; after that muscular activity. It is granted that the effect of the insulin is strengthened by an increased muscular activity. Therefore we often find that a child playing about, or engaging in football or some other kind of sport during the time of the strongest blood-sugar descent turns hypoglycæmic. On the other hand it is important to know that, as I already proved fourteen years ago, for a seriously diabetic person without insulin muscular exercise brings a rise of blood-sugar. In the child psychic factors play a greater rôle than in the adult, but I do not think that psychic influences cause the disease or even aggravate it in the long run. To the sudden change of moods of the child, to the faster reaction to joy or fright, this reaction of the blood-sugar corresponds exactly. I have often observed that such an influence causes a considerable glycosuria for one night or even a few hours of the day, which disappears the next day without changing the quantity of insulin.

However, contrary to usual surgical advice, chronic cholecystitis may, in approximately one-third of the patients, be successfully treated along medical lines. The risk of developing a surgical emergency or calamity while under medical treatment, is not greater than is the risk in the best elective gall-bladder surgery. Patients who have allowed their gall-bladder symptoms to go on for a number of years until their gastric acids have become low or absent, with definite and permanent pathologic process of the liver and biliary ducts, cannot expect as complete relief from cholecystectomy as if they had accepted immediate operation. Hence we believe emphatically that when medical management fails to relieve promptly then operation should be urged on the patient. We wish to emphasize the fact that patients with acute cholecystitis, empyema, jaundice or carcinoma have not been included in this study.

Remarks on Tuberculin in Diagnosis

By S. LYLE CUMMINS, C.B., C.M.G., M.D.

(Abstracted from the *British Medical Journal*, 7th December, 1932, p. 1089)

By the use of the original von Pirquet technique it was found that non-tuberculous persons proved to be quite as sensitive to tuberculin as the known cases. The conclusion drawn was as follows:—

The practical point at issue in diagnosis is the presence or absence of active disease. Surface vaccination is quite unreliable as a means of answering this question.

Later, with the introduction of the Mantoux intradermal technique, I decided to try out this method as one perhaps better calculated to differentiate between stages of tuberculous infection, and in 1928 and 1929 I applied the intradermal method both in healthy adults and in known cases of tuberculosis, comparing the results both as to end-point of tuberculin dilution causing reaction and actual size of reaction area. In these tests, the interesting fact came to light that the reactions tended to be, on the whole, more definite and the sensitivity more marked in non-tuberculous adults than in the tuberculous. A further comparison was made during 1929 and 1930, and the intradermal reactions to serial dilutions of tuberculin were studied on standard lines in 100 cases of pulmonary tuberculosis and in 100 non-tuberculous persons under treatment in the Cardiff Mental Hospital.

All these investigations tended to the same conclusion, which has been amply confirmed by numerous workers, that, as a test for 'active clinical tuberculous disease', the cutaneous and intradermal tuberculin tests are too delicate; and that 'positive' reactions elicited by these methods in adults cannot be interpreted to mean 'active' tuberculous disease. While this is true, however, the problem of the value of these cutaneous techniques in diagnosis is not quite so simple as it appeared to be when I attempted to exploit tuberculin in the diagnosis of tuberculosis in soldiers in 1909.

POSITIVE REACTION IN EARLY LIFE

It has been proved by many reliable workers that the cutaneous tuberculin sensitivity so constantly observed in healthy adults in 'civilized' and 'industrialized' communities is, as a rule, absent in infants, and that, while it tends to increase with each year of life, it is still very low in the earlier age groups except in the homes of 'open' cases of tuberculosis, where the contacts tend to give a high percentage of positive reactions even in infants and young children. This observation raises the question of the value of a 'positive' in early life, and here the answer is not so simple as in relation to adults. My own view, based, however, on an integration of the observations of others, is that a markedly positive reaction either to the von Pirquet or the Mantoux tuberculin test has a serious significance during the first year of life. There can, I think, be no doubt that sensitivity to tuberculin proves the existence of tuberculous infection; and, while we have reason to

know that infection is, in adults, not merely consistent with health, but usually present, we know also that very early infection, acquired in any considerable concentration before the tissues have had time to accommodate themselves to their bacterial environment, is very likely to lead on to severe and often fatal disease.

A recent paper by Blacklock (1932) indicates the extremely high risk of fatal tuberculosis in the case of infants heavily enough infected to harbour tuberculous lesions visible to the pathologist; and the Registrar-General's statistics show, year after year, that the death rate from this disease is exceedingly high during the earlier life periods. We should, therefore, view with grave anxiety the very early appearance of a 'positive' tuberculin response in an infant or in a child in the first year or two of life, since a 'positive' implies infection, and infection at this stage usually, though not always, implies the near approach of active disease.

A POSITIVE IN ADULTS

I have expressed the opinion several times already that a 'positive' in an adult brought up in an 'industrialized' or 'civilized' community has little or no diagnostic significance. This view, however, does not extend to 'positive' tuberculin responses in adults whose early years have been passed in communities of a 'primitive' type and, perhaps we ought to add, 'whose more recent ancestors have resided in communities with a primitive type of culture'. These adults, comparable perhaps in some respects to the earlier age groups in Europe and America, appear to develop tuberculo-allergy of a much more active variety than is common in adults in communities of an older civilization. Coming from districts which, through the industrial developments of recent years, have lately become endemic centres of tuberculous infection, African natives may possess an allergy potential far higher than what we encounter in this country, yet they are without the relatively high power of tuberculo-resistance common in adult Europeans. In such natives, a well-marked 'positive' tuberculin reaction has a much more formidable significance than elsewhere.

In Report No. XXX (vol. v) of the South African Institute for Medical Research (1932) will be found an account of tuberculin tests on South African native mine recruits on arrival for work at Johannesburg, together with the results of a 'follow-up' of the tested groups through their subsequent periods of work in the gold mines. On page 97 of the Report the results of this inquiry are set forth, and show that the incidence of tuberculosis was about five times as high among those who had given a 'positive plus' reaction than in those found negative to the dilutions used, 1 in 5,000 and over; while the mildly positive reactors were intermediate. The actual figures of incidence, based on 93,000 natives tested with tuberculin by the intradermal method, were as follows: in those recorded as 'positive plus', 1,547 per 100,000; in those recorded as merely 'positive', 633 per 100,000; and in the 'negative', 347 per 100,000. These figures can only mean that the 'positive plus' reactions were associated with active, though clinically unrecognizable, tuberculous lesions which tended to become generalized during the stress of a new and exacting occupation. This does not mean that a 'positive plus' reaction was diagnostic, even in these highly susceptible persons, of clinically active tuberculosis. It merely means that, out of 3,879 persons giving these marked reactions, sixty developed clinically active tuberculosis during the following year or so of work on the mines. The remaining 3,819 got safely through their mine contracts without being recognized as tuberculous, in spite of the repeated weighings and examinations which are in operation to detect and remove recognizable cases.

Has a strongly positive reaction any similar significance in this country? I have already expressed the opinion that in infants and young children it has this same kind of significance; that it must be taken to mean the presence of an active focus which, in early childhood, is always accompanied by danger of

generalization. In European adults, however, my own observations, as far as they go, do not suggest any such relation. Out of 100 mental cases tested with graded dilutions of tuberculin in 1929 and 1930, eight have since developed tuberculosis. Of these, one had reacted up to a dilution of 1 in 100,000, two to 1 in 10,000, four to 1 in 1,000, and one had been negative even to 1 in 500, the strongest concentration used.

Here the incidence was definitely greater among those who had been proved to possess low or negative tuberculin sensitivity; but the figures are too small to be of much importance. A far larger number have since been tested elsewhere by one of my co-workers, and it is hoped that a follow-up of their tuberculosis incidence will throw further light on the point at issue.

VALUE OF A 'NEGATIVE' IN EXCLUDING TUBERCULOSIS

So much for the diagnostic value of a 'positive' reaction to a cutaneous tuberculin test. But there arises also the question of the diagnostic value of a 'negative' in excluding tuberculosis. Recent work has gone far to prove that the diagnostic value of a 'negative' may be very great, especially in childhood. In attaching any weight to the value of a 'negative' in excluding the presence of tuberculous infection, the negative must be made as conclusive as possible; it is quite insufficient to stop short at a von Pirquet test, even with full-strength tuberculin, or at a Mantoux test with 1 in 1,000 tuberculin. Many persons negative to these concentrations are, in reality, positive if tested intradermally with 1 in 100 or 1 in 10.

There is another aspect of 'negative' findings, however, which deserves notice, especially in regard to adults—namely, the loss of tuberculin sensitivity which goes with advanced tuberculosis. This is hardly likely to introduce practical difficulties in diagnosis, as the nature of the disease is usually beyond doubt at the advanced stages in which the test may become negative. But if the word 'diagnosis' be extended to include prognosis, then cutaneous and intracutaneous tests may be said to have some significance, though only in the terminal stages. It does not appear that tuberculin sensitivity is ever absolutely lost until the very end, but there is a gradual fading of sensitivity, affecting both the intensity of the reaction to strong concentrations and the end-point of reaction to graded dilutions, as the resistance of the patient wears out under the stress of progressive disease. This fading of tuberculin sensitivity should, I think, be definitely distinguished from the desensitization which may arise in the course of a successfully resisted infection or through tuberculin therapy; a desensitization which is, in my opinion, to be associated rather with the acquisition of immunity than with loss of resistance.

I recently tested by the Mantoux technique six patients who had been under treatment for considerable periods, all of whom had arrived at a toleration of large doses of bacillary emulsion given subcutaneously. In one, the Mantoux test was completely negative in every dilution down to 1 in 500, the strongest concentration used. Four were negative to 1 in 10,000 but weakly positive to 1 in 1,000, that is to say, less sensitive than is commonly the case in tuberculous persons of their type. One, however, although he had received a subcutaneous dose of 0.7 c.mm. of bacillary emulsion a week earlier without reaction, experienced a sharp constitutional as well as a marked local reaction to about 1.1 c.mm. of old tuberculin intracutaneously. Apart from this anomalous case which was apparently tested just at a moment of raised tuberculin sensitivity, treatment with tuberculin had definitely lowered the allergic potential of these patients, yet all of them were doing well and in no sense 'terminal' cases.

F. Allen, testing native mine workers at the Witbank Coal Mines in the Transvaal, has observed that 'old mine workers', tested for a second time after some years of work, tend to be definitely less tuberculin-sensitive than at their first tuberculin test on arrival. Here it would seem that the repeated exposure to reinfection incident to life in the mines and in the

compounds has had the effect, not of raising, but of lowering the allergic state, though such men appear to be, on the whole, more resistant than new arrivals. One lesson appears to stand out clearly from all this South African work, with which I have had the privilege of being closely associated—namely, that while a marked positive Mantoux reaction is by no means diagnostic of clinically recognizable tuberculosis, it is to be regarded as the sign of an active, though 'larval', lesion from which infection may, under unfavourable circumstances, generalize throughout the organism. Another lesson, of greater importance from the point of view of the pathogenesis of tuberculosis, is that marked tuberculo-allergy may exist without any corresponding acquisition of tuberculo-immunity. Immunity and allergy may be due to the same cause, infection, but they are not in any sense identical or even, necessarily, coexistent.

Cutaneous tuberculin tests, then, whether of the von Pirquet or the Mantoux type, or of the type of Stichreaktion of Epstein, are reliable tests for allergy, and, by implication, for infection; but they are not of much value as tests for clinically active tuberculosis in adults nor as tests for the existence of acquired immunity.

KOCH'S SUBCUTANEOUS TEST

There remains, however, the subcutaneous tuberculin test as originally devised by Robert Koch. This test is definitely inapplicable to persons with pyrexia, a fact which greatly limits its utility in differential diagnosis; nor is it safe as a test in persons likely to be harbouring lesions of the easily activated type. In such persons, focal and general reactions are things to avoid, and there is no justification for exposing them to the risks incidental to activation of their lesions for the sake of an added point in the search for a diagnosis. There is one type of case, however, in which the risks are minimal and the advantages to the patient sometimes sufficiently important to justify the subcutaneous test. I refer to the chronic, productive, inert, sputum-negative cases which often come to our notice as ex-soldiers seeking to establish a claim to continuance of pension. These chronic and resistant cases stand the subcutaneous test well as a rule, and the risk is not serious. Koch's opinion was that a positive reaction to a dose of 10 milligrams might be regarded as diagnostic while there was no chance of a positive reaction of the general or pyrexial kind in a healthy person until the limit of 25 milligrams was reached. These quantities are, perhaps, expressed too exactly, and, in the light of modern experience, most of us will hesitate to draw the line sharply between tuberculous infection of a degree consistent with health and tuberculous infection just severe enough to constitute disease. But, of all the tuberculin tests, the subcutaneous method of Koch remains the most valuable in diagnosis. It depends upon general and focal reactions which are, in themselves, evidence of active disease, and, when elicited by tuberculin, may be accepted as diagnostic of clinically active tuberculosis. The only thing against it is its risk, and, in my opinion, there is no excuse for taking any avoidable risk in the attempt to establish a diagnosis.

I have indicated one kind of case in which Koch's original test may be applied with safety, and there are doubtless fairly numerous cases in which the subcutaneous test may be used without ill results by experienced physicians. Apart from these, it appears to me that the Mantoux test, applied with due skill and interpreted with discretion, is calculated to give valuable information, whether positive or negative, in the earlier years of life, and that apart from the diagnosis of clinically active tuberculosis, this test is invaluable as a means for determining the distribution of infection in communities in which epidemiological investigations are contemplated. On the whole, for purposes of diagnosis in man, the tuberculin test, in all its varieties, is definitely inferior to the combined radiological, physical, and laboratory examinations which have come to be the routine methods.

Reviews

DISEASES OF THE HEART.—By Sir Thomas Lewis, C.B.E., F.R.S., M.D., D.Sc., LL.D., F.R.C.P. London: Macmillan and Co., Ltd., 1933. Pp. xx plus 297. Illustrated. Price, 12s. 6d.

In these days when the medical publishers of Great Britain and the United States provide us with an average of two or three new books or new editions a day, it is not very often that one is able to say 'This is the book I have been waiting for'; Sir Thomas Lewis's book on diseases of the heart provides us with this opportunity. It is a book that every student should read when he is 'clerking' in the medical wards. On the other hand it is a book from which the practising physician will get very great benefit. It gives a very clear statement of the present-day conception of heart disease. Those who first entered the medical wards of their hospital twenty years or so ago will remember how they plunged into systolic murmurs, presystolic murmurs, and valvular incompetences and stenoses, how when they could time a murmur and percuss out the cardiac dullness they felt that the diseased hearts of the world were at their feet, and how a year or so later they were alarmed by their younger colleagues' glibness in discussing electrocardiograms which they themselves were always afraid of holding upside down. This is all changed now, and even the electrocardiograph has been made to take its place; in this book it occupies a modest place, considering the important part the author has himself played in furthering the science of electrocardiography. The emphasis in cardiology has been transferred from anatomy to physiology, and the stethoscope does not play such an important rôle in the diagnosis and prognosis of heart disease as it did some years ago.

The following extract is taken from the preface: 'I have become more and more convinced of the need for simplicity; and it was apparent that little of the graphic work could profitably be taught to men entering practice, whose foremost interest must be in observations they themselves can make upon their patients..... I have tried to strip my subject of intricacies and redundancies, of unnecessary technical terms, named signs, and old trite phrases, for these begin to stifle Medicine'. One cannot say more in praise of the book than that the author has maintained these principles throughout. We will add that the book is surprisingly cheap for one of its size and quality.

APPENDICITIS: ITS ÆTIOLOGY AND PATHOLOGY.

—By L. Aschoff. Translated by G. C. Pether, M.D., M.R.C.P. London: Constable and Company, 1932. Pp. vii plus 153, with 36 illustrations. Price, 16s.

PROFESSOR ASCHOFF puts forward in this monograph his views on the pathology of appendicitis. He has approached the subject from the bacteriological and histological point of view, and he includes a critical review of previous bacteriological investigations. In conducting his own investigations, he has devised a technique of his own. The book should be read by all bacteriologists, whose work is concerned with appendicitis or examination of surgical specimens.

His investigations are mainly concerned with appendicitis as it appears in Germany, and therefore possibly differ from the conditions found in England. His last chapter in the clinical investigations is perhaps the most interesting to surgeons and general practitioners. His evidence is obtained from 1,000 cases, the majority of which were examined histologically by himself. The main interest lies in the fact that in these 1,000 cases, the clinical diagnosis has been checked with exact histological examinations on a uniform plane.

I do not think it will be suggested that German surgeons are less careful than their colleagues in the rest of the world, and it should therefore be matter for

very serious consideration to surgeons that only 75 per cent. of cases diagnosed as acute appendicitis presented pathological evidence of the disease. Professor Aschoff suggests the use of the term 'pseudo-appendicitis' to describe the other 25 per cent. To those who discouraged the use of the term he replies 'As soon as one knows what has actually happened in these patients, one will of course be able to use the correct term'.

His findings on chronic appendicitis are equally calculated to promote modesty in surgeons. Only 50 per cent. of the cases operated on for this condition showed signs of inflammation. Here we have ample justification for those who advocate a complete examination of the abdominal viscera through an adequate incision when a diagnosis of chronic appendicitis has been made. The very popular McBurney incision is entirely unjustifiable in the so-called chronic cases.

On the other hand, he justifies the routine removal of the appendix in the course of abdominal operations for other conditions, by finding evidence of disease in over 33 per cent. of cases where no clinical evidence was noted.

Finally, there is one extract every surgeon should bear in mind before lightly advising operation for appendicitis. 'One should not underestimate the pain which may be caused by the scars or adhesions which have followed operation'.

Professor Aschoff's monograph is mainly of interest to bacteriologists, but his last chapter on clinical applications constitutes a very serious indictment of modern surgery. It is all the more serious in that nothing is further from the author's intentions.

A. H. P.

A SHORT PRACTICE OF SURGERY. Vol. II.—

By Hamilton Bailey, F.R.C.S. (Eng.), and R. J. McNeill Love, M.S. (Lond.), F.R.C.S. (Eng.). London: H. K. Lewis and Co., Ltd., 1932. Pp. viii plus 475. With 349 illustrations of which 58 are coloured. Price, 20s.

THERE are so many excellent textbooks of surgery now available that a new one has to justify its appearance by presenting the subject in a new light or appealing to a class of reader not yet catered for. It is generally agreed that the standard textbooks have grown too big and that there is room for a smaller one, which will present the subject in a simplified form to enable junior students to lay a sound foundation of knowledge of principles and of the lie of the land before plunging into the forest of detail which the larger works, with an eye on the higher examinations, invite him to try to absorb. The present work certainly does not fill this gap, as it contains very little surgical anatomy or pathology, no morbid histology and the presentation of the subject lacks the systematic form so necessary for students. One must conclude that the authors are writing for practitioners, and as a brief clinical review the book is excellent. There are short snappy descriptions of symptomatology, with an abundance of those 'good tips' which readers of Mr. Bailey's other works will expect; the fat female of 40 suggests all sorts of things besides gallstones, depending on one's line of practice, but how many readers know why they should beware of the man with a glass eye and an enlarged liver? The common conditions affecting each region are dealt with first and then the rarer diseases in small type, a sound method had a better sense of proportion been shown in the allotment of space. Brief notes on such subjects as hepatoptosis, sarcoma of the stomach, aneurysm of the splenic artery, actinomycosis of the liver, mesenteric cysts, cystic pneumatosis of the small intestine, to mention only a few of the rare conditions referred to, are of doubtful value in a book which purports to be only a brief survey, and, when one finds that the symptoms of chronic cholecystitis are dealt with in seven lines and those of chronic duodenal ulcer in half a page, one feels that the space might have been more usefully employed for fuller descriptions of

common conditions. The sections on treatment are generally very brief, with no operative details, but this is not always so, the chapter on appendicitis is very full and the Ochsner-Sherren treatment, which is advised for cases of over 48 hours duration, is discussed in detail. There is a long and excellent account, one of the best we have seen, of the subphrenic abscesses; the operations for excision of the rectum and for exposure of the brain by an osteoplastic flap are described in considerable detail, but there is no description of the operation of gastro-enterostomy, though its complications are discussed. The chapter on thoracic surgery is a brief and thoroughly up-to-date survey of the subject and the diagnosis of hernia is well described and beautifully illustrated. At the end of the book are the chapters which usually come near the beginning, those on infections and tumours, and here we find no details of the courses of treatment for syphilis, mercury advised as the adjuvant drug and bismuth stated to be useful in patients who show intolerance to arsenic. Inequalities such as these are very serious blemishes in a book whose get-up and beautiful illustrations give it a very attractive appearance. The style is crisp and pleasant to read, but the price of the two volumes and the limitations pointed out will prevent it competing very seriously with the existing popular books.

W. L. H.

COLONIC IRRIGATION.—By W. Kerr Russell, M.D., B.S. Edinburgh: E. & S. Livingstone, 1932. Pp. ix plus 191. Illustrated. Obtainable from Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 7-14.

THE introduction calls attention to the casual way in which most people, including doctors, treat constipation.

Then follows a most interesting account of the origin and gradual development of clysters or enemas, from before 1500 B.C., through the middle ages to the present day.

One theory of the origin of enemas (quoting Pliny's account) is as follows:—It is said that a certain bird, similar to the stork, called the ibis, and peculiar to Egypt, showed man the secret of lavages, because when it wants to evacuate, it syringes the anus with its beak filled with water from the sea.

The clyster reached the height of its popularity during the early years of the reign of Louis XIV. Society women found that it was an effective method of improving the complexion, and the treatment became a fashionable craze in Paris, many persons having as many as three or four treatments a day. It is stated that Louis XIV often received ambassadors and courtiers while seated on his commode. He had over 2,000 injections during his lifetime. The giving of a clyster to Louis XV was however a court ceremony attended with suitable pomp and ceremony by all the members of the Faculty!

Large numbers of similarly interesting historical facts are given in the first part of the book.

Following this is the rather dry anatomy and physiology of the colon, and then the bacteriology.

Most of the well-known types of apparatus for colonic lavage are then minutely described and also their methods of use. This section could be condensed a lot, without loss of efficiency, as it is mainly an endless repetition in varying words of the same principle. The solutions in most common use and prescriptions for making them, followed by the dangers of the treatments are then given. The book ends up with the conditions benefited. Needless to say nearly every known disease is included. Appended is a useful bibliography and index.

One feels after reading this monograph that purgative and laxative drugs should be abolished forthwith, and that their place should be taken by a douching or irrigating apparatus in every bathroom, if one is to preserve one's health!

A very entertaining book in its opening chapters and full of useful information in the remainder. Well worth reading by everyone who orders enemas to be given—and which doctor does not?

J. F. C.

MASSAGE AND REMEDIAL EXERCISES IN MEDICAL AND SURGICAL CONDITIONS.—By N. M. Tidy. Bristol: John Wright and Sons, Ltd., 1932. Pp. xii plus 429. Illustrated. Price, 15s.

THE present-day surgeon and physician, but especially the surgeon, must have a working knowledge of the many aids to treatment available under the wide inclusive term of 'physical therapy', if he is to give his patients the full benefit of modern knowledge. Most medical schools give no training in the subject at all and the massage department is looked on by students, house-surgeons, and, one is ashamed to say, many older members of hospital staffs also, as a fit place to send all the old 'chronics'. That this is absolutely wrong cannot be denied, but one usually finds that the youngest department always has the 'junk' thrust upon it in the hope that the 'new-fangled' and only half-understood treatments will succeed where ordinary treatment has failed. And the surprising thing is that these old chronics are improved, mainly by the patience, perseverance, and common sense used in the physical therapy department.

This book, besides dealing with treatment by massage and remedial exercises alone, as the title suggests, gives a concise account of almost every known medical and surgical disease, as almost all can be benefited by exercise of some part of the body. The ætiology, pathology, and symptoms are all accurately and shortly described, and then follows treatment which is dealt with very fully. Instructions are also given as to the length of time it is usually advisable to persist with treatment in any particular case. As the author states in the preface her aim has been to provide most details where other books provided least. In this she has definitely succeeded. In fact many well-known medical and surgical textbooks might with advantage amplify their sections on treatment by passages from this book.

The book will be invaluable to all massage students, teachers, and practitioners, and could be read with advantage by all keen medical men who wish to gain new ideas in treatment which, in most textbooks, is dismissed in one word—massage.

The illustrations and general arrangement of the book are excellent.

J. F. C.

SURGICAL ERRORS AND SAFEGUARDS.—By Max Thorek, M.D. Philadelphia and London: J. B. Lippincott Co., 1932. Pp. 696, with 668 illustrations. Obtainable from Butterworth and Company (India), Ltd., Calcutta. Price, Rs. 33-12.

As the author points out in his preface, there is no shortage of surgical textbooks to tell us what to do and how to do it, but it is seldom that they tell us what not to do, how to avoid complications and technical errors, and how to act when face to face with some of the abnormal circumstances that so frequently present themselves during the course of an apparently routine surgical operation. Scattered descriptions of mishaps and accidents exist throughout the literature, but this is, so far as is known, only the second occasion on which an effort has been made to arrange them systematically in one volume.

As it is not often that unsuccessful cases are placed on record, the collection of the material for this book must have involved considerable and painstaking work. A regional arrangement has been adopted, sections dealing with anaesthesia, pre- and post-operative treatment, the treatment of the 'bad risk' case and a chapter on gynaecology being included. On the whole the subject has been treated in a practical and instructive manner, though here and there one notices that redundant matter has been included, making the book

rather unwieldy without adding to its usefulness. The illustrations are also rather more numerous than is justified by the text. If the work reaches a second edition, the author would be well advised to curtail its size.

The publishers are to be congratulated on the clearness of the type, reproduction of the illustrations and the general presentation of the book.

J. C. D.

COMMON SKIN DISEASES.—By A. C. Roxburgh, M.A., M.D., B.Ch. (Cantab.), F.R.C.P. (Lond.). London: H. K. Lewis and Co., Ltd., 1932. Pp. xxx plus 322, with 8 plates in colour and 110 illustrations in the text. Price, 18s.

This book is one of the volumes that have been published in the General Practice Series. The author is physician in charge of the Dermatological Department of St. Bartholomew's Hospital and has been able to present the wealth of his large experience in a simple and concise manner for the benefit of the student and practitioner.

At the beginning of the book Dr. Roxburgh gives an index of the lesions to help in the preliminary diagnosis of these diseases; this index although not, in the reviewer's opinion, strictly accurate will be of the greatest help to the student in his early study of dermatology. The skin diseases are divided into sections according to their causation—a very good method of classification. The illustrations, consisting of 8 coloured plates and 110 half-tone figures in the text, are very good.

As an introduction to the study of dermatology, this is the very best book that we have encountered for many years; we can strongly recommend it to the student or practitioner, and the price is moderate.

H. W. A.

AN INTRODUCTION TO DERMATOLOGY.—By R. L. Sutton and R. L. Sutton. St. Louis: The C. V. Mosby Company, 1932. Pp. xvi plus 565, with 183 illustrations. Price, \$5.00.

This book has been written by the well-known dermatologist, R. L. Sutton, in conjunction with his son, and is very well illustrated by 183 half-tone plates. Each disease is treated in a brief and concise manner—this will appeal to the student. The volume is really a digest of the elder Dr. R. L. Sutton's well-known textbook on diseases of the skin. The authors have succeeded in their object, and the book can be recommended to those who require a short and concise account of these skin diseases.

H. W. A.

DISEASES OF THE EYE.—By A. Rugg-Gunn, M.B. (Edn.), F.R.C.S. (Eng.). London: William Heinemann (Medical Books), Ltd., 1933. Pp. xli plus 188. Illustrated. Price, 12s. 6d.

In English-speaking countries there are so many textbooks for undergraduates of medicine to gain their knowledge of ophthalmology from that one is surprised at the appearance of yet one more. The book, however, is written primarily for the use of the general practitioner. It includes a description of all the more common types of eye disease with a simple, concise account of their pathology and with special attention to the principles of treatment that he is likely to come across in the course of his practice. In India, where so much eye disease abounds everywhere, this knowledge is all the more important, and if only the more serious forms of eye disease could be diagnosed early by the general practitioner, how much less the incidence of blindness would be. It is pathetic, but nevertheless true, that so many eyes have been lost by such diseases as glaucoma and corneal ulcers, and all from a lack of a simple knowledge of the principles of ophthalmic treatment.

The contents of this small book consist of twelve chapters arranged according to an anatomical classification with an appended materia medica of the majority

of drugs used in ophthalmology. In addition there are 8 plates and 21 figures in the text, all of which have been specially drawn for the book. It is unfortunate that a whole page should be devoted to the medical treatment of cataract which is of very little use and might well be omitted, as likely to mislead the general practitioner.

The work undoubtedly supplies a want. It is written in a clear, concise and simple style which can be easily understood by the general practitioner, who will find in it a wealth of practical information. We strongly recommend the book and, as its price is very moderate, it should find a place in the library of the medical man working in India.

E. O'G. K.

MEDICINE: ANALYTICAL REVIEWS OF GENERAL MEDICINE, NEUROLOGY AND PEDIATRICS. Volume XI, December, 1932, No. 4. Baltimore, U. S. A.: The Williams and Wilkins Company. Pp. from 371 to 535. (English Agents are: Baillière, Tindall and Cox, London.) Price, 21s. per volume and postage 2s. 6d. Single Copy 6s. 9d.

This journal has already made its mark as a first-rate journal dealing with general medicine, neurology and pediatrics, and the editorial board deserves congratulation for consistently keeping the standard at such a high level. The December number of volume XI is likely to be of special interest to clinicians and physiologists.

The first article deals with the adrenal cortical hormone. The function of the adrenal cortex is not definitely known at the present time, though various theories have been advanced. An attempt has been made to obtain an active preparation of the suprarenal cortical hormone and by means of it, to study adrenalectomized animals, subjected to various dosage over long periods. The hormone has also been given extensive trials in various types of cases, including Addison's disease, in the Mayo Clinic. Though no definite statement can be made with regard to the function of the suprarenal cortex, this piece of research would go a great way in advancing our knowledge about the physiology of the gland.

The second article presents in a masterly manner the salt and water metabolism in nephritis, a subject which has remained debatable to this day. The causation of oedema in nephritis has been frequently explained on the basis of salt retention alone, but the explanation is not as simple as is generally believed. The subject has been taken up from all angles of approach, and it will form very illuminating study to all those interested in experimental medicine and physiology. The bibliography at the end of this chapter is worth special mention.

R. N. C.

THE ORGANS OF INTERNAL SECRETION.—By Ivo Gekkie Cobb, M.D., M.R.C.S. Fourth Edition. London: Baillière, Tindall and Cox, 1933. Pp. xlii plus 303. Price, 10s. 6d.

The literature on endocrinology has grown enormously in recent years so that it is difficult for anyone not engaged in teaching or research work on these or allied subjects to obtain a comprehensive view of the facts upon which modern ideas are based. As the use of organic preparations is now an established method of treating disease and one which will undoubtedly form a large part of treatment in the future, the general practitioner has always been on the look-out for a treatise which will give him the essential features of the subject without going into too much academic detail. In the fourth edition of Dr. Cobb's book, he will get a book answering his requirements. It is a book of moderate size, full of up-to-date information on practical points. The physiological and pathological aspects of the different ductless glands have been briefly discussed and the rationale of their therapeutic application in diseases explained. A chapter on obesity

with special reference to its relation to the endocrines is given. In the chapter on the application of the hormones, a list of the various gland preparations available in the market is appended. This will be of great help to practitioners in prescribing the gland preparations.

R. N. C.

ACIDOSIS AND ALKALOSIS.—By Stanley Graham, M.D., F.R.F.P.S., and Noah Morris, M.D., B.Sc., D.P.H., F.R.F.P.S. Edinburgh: E. & S. Livingstone, 1933. Pp. xii plus 203. Illustrated. Obtainable from Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 5-10.

DURING recent years, the disturbance of the acid-base equilibrium in the body is being more and more widely recognized as an important factor in the causation of disease. Within the last 50 years, a good deal of research work has been done which has helped to throw light on this difficult physiological and chemical problem. It has, for instance, been generally accepted that for the organism to be maintained in a state compatible with life, the reaction of the inner fluids must be slightly alkaline and that much deviation from the physiological point of neutrality is disastrous. The factors contributing to the maintenance of this physiological state of neutrality in the system are very complicated indeed.

Owing to intensive work done within the recent years, evidence is accumulating which goes to show that a disordered metabolism arising out of or leading to a disturbance in the acid-base equilibrium is the cause of many morbid conditions and that many of the phenomena in disease are manifestations of the body's activity in preventing a change in the reactions of its fluids.

We welcome the laudable attempt of the authors to present a general survey of this very intricate subject in a comparatively simple and easy way. The subject is a highly scientific one bristling with complexities and technicalities. For its thorough understanding, not only a knowledge of higher mathematics and chemistry, but also of bio-chemistry and bio-physics, is necessary. The authors have avoided discussions on controversial problems and have put the general outline of the subject, specially in its relation to the causation of disease, in a clear, concise and cogent way, which, we hope, will be of great help to those who are making higher studies in clinical bio-chemistry.

J. P. B.

INFLUENZA: A CLINICAL LECTURE.—By T. B. Layton, D.S.O., M.S. (Lond.), F.R.C.S. (Eng.). London: Ash and Co., Ltd., 1933. Pp. 35. Price, 1s.

THIS little pamphlet, written by a well-known London throat specialist, should prove very useful to the busy practitioner during an influenza epidemic, and we can strongly recommend it as a book to be slipped into the pocket and read in one's car during the morning round. There are many features that appeal to the reviewer, but the writer's advice on the subject of alcohol in acute disease has made the most permanent impression; he warns us that it should be presented aesthetically, and he suggests that champagne out of a medicine glass is not the same as champagne out of a champagne glass. This is true to a certain extent, but it is mainly applicable where the patient has a taste for champagne and is used to drinking it out of the orthodox glass. Similarly, good advice on the subject of influenza is good advice in whatever form it is given, but some readers find it more palatable when the writer has taken a little extra trouble over its presentation.

The author says 'It (influenza) is probably a virus disease due to some ultra-microscopic living organism that can pass through a filter which will hold up anything large enough to be seen with such microscopes as have yet been invented', and he is probably right.

L. E. N.

FAVOURITE PRESCRIPTIONS.—By E. Ward, M.D. (Belfast). Third Edition. London: J. & A. Churchill, 1933. Pp. viii plus 148. Price, 7s. 6d.

THIS is one of these invaluable little books that contain all the information a prescriber can possibly want. The publication of the new pharmacopœia has stimulated writers and publishers of these prescription books to produce new editions, and we have received many for review. The present volume seems to be as complete, as concise and as suitably printed and bound as any we have seen. The changes in the new pharmacopœia, such as the new inclusions, the exclusions, and the changes in strength and dosage of various drugs, are indicated by stars and crosses, without addition to the bulk of the volume. There is a useful section on the treatment of poisons, and another on dietary; the latter provides the only criticism we can make. A dietary table for a disease like diabetes is of course very helpful, but can one prepare tables for conditions like anæmia and eczema, clinical manifestations with such manifold ætiologies? The greater part of the volume consists of useful prescriptions; these all appear to be very sound indeed. It is a book that deserves a wide sale.

THE RISE OF PREVENTIVE MEDICINE.—By Sir George Newman, K.C.B., M.D., F.R.C.P., Hon. D.C.L., LL.D. Oxford University Press, London: Humphrey Milford, 1932. Pp. 270. Price, 10s. 6d.

THE history of preventive medicine is essentially the history of medicine as a whole; the highest aims of physicians of all times have been prevention rather than cure. The tide, from century to century, has now flowed towards prevention and has then ebbed towards cure. Sir George Newman, himself one of the greatest living exponents of the practice of preventive medicine, has here given us as connected and concise a history of the birth and growth of the science of medicine as one could wish to read.

The reading of a history like this is very good for our sense of proportion; we are inclined to think that the advances that have been made in our own time are prodigious. From our point of view, the man who has been away from all practice for 20 years would find himself entirely out of date in many matters, but in a thousand years time, or even in a hundred, will the contrast between 1913 and 1933 be so very great? The early papyri show that practice in those days consisted of a mixture of magic and medicine; to-day many of our patients still believe that warts can be charmed away, and Harley Street is not entirely free from magic boxes. A thousand years before Christ the opinion was current in Egypt that 'every disease is occasioned by dietary'; we believe that this opinion is still maintained, and with good reason in Coonoor to-day. And so we progress.

The reviewer has always held the opinion that specialization in medical practice is of comparatively modern origin; he is pleased to see that this book confirms his opinion—provided a sufficiently wide interpretation is given to the word 'comparatively'. There does not seem to be any reference to specialization during the First Dynasty or even at the time of the Ebers papyrus, but in much more recent times Herodotus (500 B.C.) recorded that in Egypt they were more advanced than in other parts of the world and that there 'each physician treats a single disorder and no more'. He also found that to avoid 'gnats' the people lived in high towers, or used nets; so even they had their Ronald Rosses!

However, there have been many lapses since those times, and in England it took the Black Death and other similar expensive lessons to start us on the path of preventive medicine again. The book takes us up to the time of Sir John Simon; the next chapter might well be entitled 'From Sir John Simon to Sir George Newman', had it been written.

L. E. N.

MANUAL OF HYGIENE AND PUBLIC HEALTH.—By Ral Bahadur Jāhar Lal Das, D.P.H. Third Edition. Calcutta: Butterworth and Co. (India), Ltd., 1932. Pp. xxi plus 661. Illustrated. Price, Rs. 3-8.

THAT a third edition of this manual has been called for since 1925 is proof that it fulfils a definite demand. It presents in clear and simple language the salient facts of public health considered necessary by the author for medical students. It will be found useful for reference by public-health students, though it would naturally require to be supplemented by wider reading. One or two points we might suggest for the next edition. In a student's manual it is useful to give a scale of measurements so that an accurate idea of the dimensions of the objects illustrated is obtained, e.g., on p. 436, the adults and embryo of the ankylostoma are shown as approximately of the same size, and no indication of the natural size is given; and again the illustration on p. 437 of the hook-worm larvæ penetrating the skin, suggests something of the size of an earthworm entering a large hole in the sole of the foot. The same remarks apply to the pictures of tape-worms on p. 428, to the helminth eggs on p. 429, and to the various pictures of insects.

Neither in the description of the sand-flies nor in the chapter on kala-azar is there any mention of *Phlebotomus argentipes*, and its possible relationship to the transmission of kala-azar. Some precise information on the work that has been done in India in this connection should surely have been included, without necessarily committing the author. In the prophylaxis of kala-azar no mention is made of treatment centres, but measures of segregation alone are suggested. It is stated on p. 560 that 'Koch maintains that human tuberculosis is different from bovine. He further holds that bovine tuberculosis is not dangerous to man'. In fairness to a great figure departed, it should be stated that Koch very definitely receded from his earlier views.

The chapters on refuse and sewage disposal, water, food, soil and housing are very good; but that on vital statistics is too compressed for clarity. There are useful and helpful sections on fairs and festivals, and on camp sanitation. Several appendices are incorporated giving the duties of medical officers of health, rules regarding food adulteration and the salient features of various public health acts. One appendix gives a synoptic table for the identification of Indian anophelines.

The price, Rs. 3-8, is marvellously low, though the paper and binding have had to be sacrificed somewhat; the reviewer's copy is marred by a large number of pages of unbleached paper. Nevertheless the book is excellent value for the money, and is practical and useful in its outlook and treatment.

EPIDEMIOLOGY IN RELATION TO AIR TRAVEL.

By A. Massey, M.D., D.P.H. London: H. K. Lewis and Co., Ltd., 1933. Pp. vii plus 59, with 5 maps. Price, 7s. 6d.

THE appearance of this small book is opportune for, as far as we are aware, apart from reports of conferences this is the first publication of its kind, dealing with a problem in epidemiology that is relatively new to the world and is becoming almost daily of greater importance.

Most of the diseases discussed are naturally tropical in their incidence, and, as the book is written by a health officer of an inland English city, much of the matter is necessarily sketchy, and we cannot agree that the Asiatic distribution of plague and cholera are practically identical, as two of his maps suggest.

But, apart from slight errors in detail, the book is a valuable one as it gives a rapid résumé of the essentials regarding the danger of the spread of disease by aeroplane, and also indicates reasonable precautions that may be taken to prevent this; it is therefore recommended to health authorities whose work brings them in touch with long-distance air traffic.

NUTRITION IN HEALTH AND DISEASE FOR NURSES.—By L. F. Cooper, B.S., M.A., M.H.E., E. M. Barber, B.S., M.S., and H. S. Mitchell, B.A., Ph.D. Fourth Edition. Revised. London: J. B. Lippincott Company, 1932. Pp. xli plus 606, with 102 illustrations. Price, 12s. 6d. (Obtainable from Butterworth and Co. (India), Ltd., Calcutta.) Price, Rs. 9-6.

IN this book the authors have presented the principles of nutrition and dietetics in a very simple and lucid manner. It contains most of the recent advances on the subject and is quite up to date. It is divided into five parts. Part I deals with the principles of nutrition and has some very useful chapters on the value of vitamins of mineral salts in nutrition and health. Part II deals with food selection and contains very valuable hints on the preparation of suitable menus. This chapter will be found interesting by nurses. Part III deals with diet in disease. This is the most valuable section in the book and will be found useful both by physicians as well as nurses. In it the authors have discussed the dietetic treatment of disorders of the gastro-intestinal tract, diseases of the liver and biliary tract, over-weight and under-weight, epilepsy, arthritis, gout, diabetes, and allergic diseases, and have furnished some very important information. Part IV deals with the method of cooking for the sick and convalescent. It has numerous recipes and practical hints on cookery, and will be found useful by nurses. Part V deals with instructions to teachers regarding the use of the book.

Although primarily meant to supply the needs of the nurse, the book will be found very useful by the general practitioner as well. To those who are interested in the dietetic treatment of diseases the book is recommended.

K. V. K.

THE DIABETIC LIFE: ITS CONTROL BY DIET AND INSULIN.—By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Seventh Edition. London: J. & A. Churchill, 1933. Pp. viii plus 218, with 10 illustrations. Price, 8s. 6d.

THE first edition of this practical manual, useful both to practitioners and patients, was published by the author in 1925, and the fact that within a period of 8 years the book has gone through seven editions speaks volumes for its popularity. The author's object has been to bring the modern treatment of diabetes within the knowledge of diabetic patients so as to enable them to understand and follow the rationale of the treatment prescribed by the physician, in an intelligent and effective manner. In this the author has succeeded.

The present edition of the book contains up-to-date information relating to the treatment of diabetes mellitus. On account of the present practice of giving a higher carbohydrate diet, the carbohydrate content of the 'line ration scheme' has been doubled, each black line containing ten instead of five grammes carbohydrate.

The book should prove eminently useful to those for whom it is intended.

J. P. B.

A DOCTOR TO A MOTHER: THE MANAGEMENT OF MATERNAL AND INFANT HEALTH.—By E. Holland, M.D., F.R.C.S., F.R.C.P., F.C.O.G., J. C. Jewesbury, M.D., F.R.C.P., and W. Sheldon, M.D., M.R.C.P. London: Edward Arnold and Co., 1933. Pp. 96. Price, 1s. 6d.

A Doctor to a Mother comprises a series of wireless talks broadcast by well-known experts on the management of maternal and infant's health.

Dr. Eardley Holland contributes two chapters on ante-natal care which set forth clearly the reasons which make examination necessary, the scope of the examination, and the use made of the information obtained in planning a suitable regime.

Dr. Jewesbury deals with the normal baby and its dietetic and other requirements, the precautions to be

taken to maintain and promote health, and the reasons for minor departures from health.

Dr. Sheldon is responsible for three chapters on normal physical and mental development, and some of the commoner nervous disturbances which can be prevented by careful management and training.

The style is simple and lucid, the teaching excellent and while the work cannot, and is not intended to, supplant personal contact between parent and doctor, it will form an excellent background for any additional advice the doctor may find necessary. Popular books on mothercraft in the Indian vernaculars are few and far between, but the demand is increasing and a translation of *A Doctor to a Mother* with a few minor modifications would fill the gap admirably. It is an excellent little book to recommend to mothers, since it will whet their appetites for more knowledge, and will lead them to consult the doctor or the welfare centre in time to prevent disasters.

J. M. O.

THE PHYSICO-CHEMICAL THEORY OF THE PROCESS OF THE INTERNAL DEFENCE OF ANIMALS.—By D. S. Anand, M.B., B.S. Published by the author, I. D. Hospital, Lahore. Pp. xiv plus 92.

In this report Dr. David Satya Anand has attempted to convey to his readers the main principles on which modern immunology is founded. He has given extracts from several books (thirty in number) of recognized importance, including Topley and Wilson's *Principles of Bacteriology and Immunity*, and Well's *Chemical Aspects of Immunity*. These extracts occupy the major portion of the report; the last few pages of it are, however, devoted to a description of certain experiments on antigen-antibody relationship which the author claims to have performed under very trying circumstances.

The chief object of the report, according to the author's own admission, is to elicit the sympathy of the readers and to obtain financial, laboratory and other facilities for work, through their influence. It strikes one as a queer method of appeal which, although very original, cannot be called very sound. It would have been far better if the writer had utilized the money, time, and energy that he spent on the preparation of this report in performing, on an extended scale, the experiments he thinks necessary, and had then published his results in scientific journals.

The get-up of the report is fair, but there are many grammatical and other errors which could have been easily avoided.

The writer deserves every sympathy and may be complimented for the trouble he has taken in publishing this report.

K. V. K.

SWASTHYA AUR ROG. (HEALTH AND DISEASE.)

Written in Hindi.—By T. N. Varma, B.Sc., M.B., B.S., D.T.M., L.M., F.R.F.P.S. Published by the author, Allahabad. Pp. 895, with 407 illustrations. Price, Rs. 7. (Available from Law Journal Press, Allahabad.)

This book is written in the Hindi language. It deals with a large variety of subjects relating to the laws of hygiene and prevention of diseases, and is divided into 28 chapters.

Beginning with a discourse on the place of man in the universe and his struggle for existence, the author has admirably put before the readers the rôle of bacteria, flies, insects and parasites in the causation and transmission of human disease. The subjects of ventilation, housing, water, dietetics and exercise have been thoroughly discussed. All the preventable diseases have been described and the prophylactic measures advocated are sound and up to date. Other important diseases and congenital abnormalities have also been dealt with. Sound advice has been given as regards personal hygiene. Finally, a couple of chapters are

devoted to the question of sexual psychology, sex-hygiene and infant nursing.

The book is profusely illustrated. Most of the illustrations are original and the remaining ones have been reproduced from standard European books. The coloured plates are excellent and reflect credit on the printers.

The author is gifted with a charming style and the book he has written is a veritable store-house of knowledge. We have no hesitation in recommending it to the Hindi-reading public.

A. K. M.

BAILEY'S TEXTBOOK OF HISTOLOGY. Revised and rewritten by A. Elwyn, A.M., and O. S. Strong, A.M., Ph.D. Eighth Edition. London: Baillière, Tindall and Cox, 1932. Pp. xvi plus 746, with 529 figures in the text. Price, 31s. 6d.

This book is the work of a group of professors of the Columbia University. It is written primarily for the student and controversial discussions have been wisely avoided. With each new edition some chapters have been rewritten, so that since the first edition the book is completely changed. In this edition a new chapter on the living cell has been added; in it the subject of tissue culture has been dealt with at some length. The study of the living cell has, as the authors say, broken down the barriers between anatomy and physiology, and this chapter will add reality to the subject of histology from the point of view of the young student.

In the chapter on the various blood cells and their origin, the authors have taken Maximow's view of the unity of origin of the monocyte and the histiocyte, the former having undergone a change of function. They use the word 'monocyte' in place of the more comprehensive term 'large mononuclear', to include both monocyte and histiocyte; in view of the fact that they admit the difference in function of these two cells, it seems a pity thus to confuse the reader. However, they may take the view that the histiocyte does not normally appear in the peripheral blood, and it is with the normal that they are mainly dealing.

The book is clearly written and well illustrated, and it should prove a very useful standard textbook on histology.

L. E. N.

MACKENNA'S DISEASES OF SKIN. Third Edition. Revised and enlarged by R. M. B. MacKenna, M.A., M.D., B.Ch. (Camb.), M.R.C.P. (Lond.), M.R.C.S. (Eng.). London: Baillière, Tindall and Cox, 1933. Pp. xiv plus 506, with 149 figures and 45 plates. Price, 25s.

This book already enjoys an established reputation amongst students and practitioners as a useful guide to the diagnosis and treatment of skin diseases. It is of about the right length, neither an encyclopædia in which all the rarest conditions are described, nor a scrappy 'introduction' which contains too little to be of any value except to examinees. The third edition has been edited by Robert W. MacKenna's son. It is no mere reprint of the second edition; the subject-matter has been brought up to date and in most chapters reference is made to papers published since the appearance of the last edition, and, we are told, a number of new plates have been added. The book provides us with as good an exposition of the present-day practice and teaching of dermatology as one could want. The student who absorbs its contents should welcome a question on skin diseases in either his paper or his *viva voce*, and the practitioner who has it to refer to should never be at a loss to attach some Latin name to his patient's skin lesions or to find a new prescription to try.

This is as much as we can say in praise of the book; our quarrel is not with the author, but with the whole body of dermatologists. Admittedly, the subject is a difficult one, and most treatments very unsatisfactory, but the dermatologists do not even face the facts, instead

they revive a subterfuge which was discarded a hundred years ago by the more honest amongst the medical profession and cloak their ignorance by the application of long Latin names, the puerility of which they themselves are obviously ashamed. They apply dozens of different names to conditions with slightly varying clinical manifestations but obviously a single ætiology, and yet they will group together a variety of conditions with very divergent ætiologies and call them 'eczema'. The author of this book refers to the 'protean manifestations' of eczema, and the multiplicity of its causes, he gives a very vague definition, by which it would be difficult to distinguish eczema from other inflammations of the skin, and yet he maintains that it is a distinct disease; he may have reasons to justify this claim, but he does not give them.

Whilst dogmatism is to be deplored, it seems unnecessary to introduce, particularly without any guiding criticism, a whole series of little-used forms of treatment. For example, under the treatment of syphilis the following isolated paragraph appears—'Antimony is less efficacious than salvarsan, and may be used in the form of tartar emetic.....injected intravenously.....' It certainly is less efficacious than salvarsan, but what is the authority for assuming that it has any action at all on either the lesions or the Wassermann reaction?

We cannot close this review without reference to the very beautifully reproduced plates; the colours are very true. There are 45 of these, many of which have two figures; and they are alone worth the price that is asked for the whole book.

L. E. N.

Annual Reports

REPORT OF THE HEALTH ORGANIZATION FOR THE PERIOD JANUARY 1931 TO SEPTEMBER 1932. LEAGUE OF NATIONS, GENEVA.

I. PERMANENT COMMISSION ON BIOLOGICAL STANDARDIZATION

This Commission met in London on 23rd June, 1931, under the chairmanship of Dr. Madsen. Its agenda included the standardization of gas-gangrene antitoxin, tuberculin, and diphtheria prophylactics.

Following its usual custom, the Commission had invited all the experts who took part in the preliminary laboratory researches to attend its meetings. They were allotted to sub-committees as follows:

The proceedings of these sub-committees may be summarized as follows:

Gas-gangrene antitoxin.—The use of active serum against *B. perfringens*, an agent of gas-gangrene (B. of Welch-Fraenkel), has tended to become general since the war. It was therefore in the interest of practitioners and producers that its potency should everywhere be expressed in terms of the same unit. That unit had to be capable of definition in terms of a standard serum which, being prepared in a stable form in quantities sufficient for distribution amongst the producing laboratories, would enable them to adjust the potency of their own serum to that of the international standard. Hitherto an antitoxin unit had been adopted only in the United States of America, but as, in practice, that unit proved to be too large, a unit one-hundredth the size was substituted for it in 1930.

The questions which the Permanent Commission on Standardization sought to solve were the following:—

(1) Can the anti-perfringens serum be assayed with sufficient accuracy?

(2) What standard should be adopted for international use?

The Commission adopted the same method of work as had previously enabled it to reach agreement on the standards used in assaying antidiphtheritic, antitetanic and antidyenteric sera. This method consists in entrusting researches to a number of laboratories, both official and private, in the countries concerned. The experimental results are communicated to the Danish State Serum Institute, which acts as a central laboratory. When the contributions thus brought together seem to point to a solution of the problem, the experimenters are invited to a conference, at which any divergencies which may still remain are easily adjusted. This is what took place at the London meeting.

The investigations undertaken at the Commission's suggestion were based on the use of two sera in the dry state, one of which was prepared by the National Institute of Health, Washington, and the other by the Wellcome Physiological Research Laboratories,

Beckenham. The relationship between the potency of two solutions of these sera, expressed in the new American units, had been carefully calculated at the Washington laboratory. The experimenters were asked, on the one hand, to repeat this assay, and, on the other hand, to determine the activity of an antitoxin of unknown potency. To facilitate the work, they were supplied with a stable preparation of toxin.

The results obtained are in agreement. In the assay of the unknown serum, 7 workers out of 8 returned values ranging from 200 to 225 new American units per c.c. As regards the comparison of the solutions of dried sera, all the assays showed an adequate equivalence.

The dry preparations of anti-perfringens serum may therefore be prepared and assayed in terms of the American standard. The Commission was thus able to recommend:

'That the standard preparation and unit adopted in the United States of America be accepted for international use, and that the "Statens Serum Institut", Copenhagen, be requested to keep and distribute the international standard.'

Toxins used in the Schick test.—The test dose used in the Schick test was originally defined as one-fiftieth part of the minimum lethal dose, for a guinea-pig, of a matured diphtheria toxin. This definition is still in use in the United States and the dosage there is therefore based entirely on the lethal action of the toxin on the guinea-pig. It is nevertheless considered to be sufficiently accurate for the practical purpose of distinguishing receptive subjects from immune subjects.

With dosage carried out on this basis, it is clear that test doses of different toxins may contain varying proportions of toxoid to toxin, and that these test doses may therefore vary rather widely in their combining powers for antitoxin. Experimentally, it is easy to show that animals with an appropriate amount of antitoxin in the blood will give a positive reaction to one and a negative reaction to the other of two toxins varying in their combining power, though injected in both cases in equal quantities representing the same fraction of the minimum lethal dose. There remained a difference of opinion as to the necessity for a supplementary adjustment of the test dose in relation to its combining power. In some countries—e.g., the United Kingdom—this adjustment was legally enforced. This additional stipulation excluded from use many toxins which would have been available on the American basis. With a view to international agreement on a definition of the test dose, the Commission studied the question of the necessity for dosage by combining power.

The Schick test was to be carried out on actively immunized individuals, convalescent cases of diphtheria, healthy individuals who had been given diphtheria.

antitoxin as a prophylactic measure, and, finally, normal individuals. The toxins were to be injected each into one arm, and there was also a control injection with the same toxins heated to 85°C. for thirty minutes.

Of the 1,457 individuals tested, the numbers of Schick-positive and Schick-negative reactors were as follows:

	Toxin A	Toxin B
Schick-positive reactors ..	594	660
Schick-negative reactors ..	863	797

The international enquiry thus showed that the number of persons classed as Schick-positive or Schick-negative depended on the properties of the toxin used in making the test. The Commission therefore recommended that, in choosing a diphtheria toxin, its combining power as well as its toxicity should be taken into account.

Diphtheria prophylactics.—What preparation of diphtheria prophylactic, preferably an anatoxin, might be adopted as an international standard, and what fraction of that standard should be used as a unit? The Commission entrusted the study of these questions to the Statens Serum Institut, Copenhagen; the Staats-Institut für experimentelle Therapie, Frankfurt-on-Main; the National Institute for Medical Research, London; the Institut Pasteur, Paris; and the National Institute of Health, Washington.

Before the study of these questions is begun, however, experimental research will have to be undertaken with a view to ascertaining, on the one hand, the length of time which must elapse between the injection of anatoxin and the test for immunity, and, on the other hand, the importance which should be attached to seasonal variations in immunity.

When these two points have been cleared up, comparative tests on the immunizing potency of different prophylactics will be carried out in accordance with a plan of research drawn up by the Commission.

Tuberculin

The question of the standardization of tuberculin has been before the Commission since 1926. Numerous comparative assays of the standard preparations in use in the different laboratories have been carried out on various occasions, and have shown that the standards were equivalent. The Commission was therefore able to recommend that the preparation of tuberculin kept at the Statens Serum Institut, Copenhagen, should be accepted as a standard for international use. The testing may be carried out by subcutaneous or cutaneous injection.

The Commission was of opinion that the question of the standardization of anti-meningococcus and anti-pneumococcus serum could not usefully be pursued at present. On the other hand, it decided to undertake a study of the standardization of sex hormones, more particularly the oestrus-producing hormone, and of certain biological products used for veterinary purposes.

To the list of products for the standardization of which it has been possible to reach international agreement under the auspices of the Commission on Biological Standardization, there have thus been added gas-gangrene (*perfringens*) antitoxin and tuberculin, in addition to the vitamins, to which reference is made below. This represents valuable progress by which practitioners and manufacturers will benefit.

CONFERENCE ON VITAMIN STANDARDS

The problem of the standardization of vitamins was taken up in 1925 by the Second International Conference on the Standardization of Biological Products, which requested Professor Poulsen to undertake a critical examination of the whole question. He reached the conclusion that only the assay of the growth-promoting factor in vitamin A might at that time have formed the subject of international agreement. Since then, our knowledge of vitamins has increased, and the time seemed to have come to resume the study of this question. A Conference on Vitamin Standards was

accordingly held in London from 17th to 20th June, 1931, under the chairmanship of Dr. E. Mellanby, Professor of Pharmacology, University of Sheffield.

At the outset, the Conference decided that, in the present state of our knowledge, the study of the fat-soluble vitamin A, the antirachitic vitamin D, the antineuritic vitamin B, and the antiscorbutic vitamin C might profitably be undertaken. It had also to take a decision on a question of principle: should the vitamin units be defined with reference to their biological action, or should they be expressed as a definite weight of the standard? The second alternative was adopted, this being in line with the precedents set by the earlier conferences, which resulted in the standardization of digitalis, strophanthus, insulin, salvarsan, and pituitary extract.

In regard to the *fat-soluble vitamin A*, the Conference recommended that, for two years, carotene should be accepted as an international provisional standard of reference, and that cod-liver oil should be held in view as a possible secondary standard.

The preparation of carotene, extracted from carrots by Willstätter's method and purified by recrystallization, will be a mixture of the two isomers the biological activity of which appears to be similar. A sample of carotene prepared in the laboratories of the countries concerned will be sent to the National Institute for Medical Research, London, which, acting as the central laboratory on behalf of the Health Organization, will be asked to undertake the final preparation of the international standard, the unit of vitamin A being equivalent to 1 milligramme of that standard.

No particular method was recommended for conducting the assay, since further progress seems to be necessary in the study of methods based on the curative action of carotene in xerophthalmia. Moreover, it is highly desirable that investigations should be made regarding the stability of carotene, both when sealed in tubes and when in solution.

The Conference decided to ask the Department of Agriculture of the United States of America to place at the disposal of investigators in other countries sufficient supplies of cod-liver oil to enable them to assay this oil in terms of the standard preparation of carotene. It is hoped thus to obtain evidence regarding the stability of vitamin A in cod-liver oil as affected by the conditions in which that oil is stored.

By a decision of the Conference, the standard for the *antirachitic vitamin D* will, for the next two years, be the solution of irradiated ergosterol at present issued from the National Institute for Medical Research, London. If, owing to the exhaustion of the reserve, it became necessary to replace this solution by a fresh standard, the equivalence of the two products would be determined by experts belonging to the following institutions:—

- Allgemeines Chemisches Laboratorium, Göttingen;
- Tierphysiologisches Institut, Leipzig;
- Food and Drugs Administration Laboratory, Department of Agriculture, Washington, D.C.;
- Biochemical Department, University of Stockholm;
- Department of Agricultural Chemistry, University of Wisconsin;
- School of Hygiene, Johns Hopkins University, Baltimore;
- Laboratoire de Physiologie de la Nutrition, École des Hautes Études, Paris;
- Pharmaceutical Society, London.

In the preparation of the future standards, irradiation with ultraviolet light must be done in ethereal solution in the absence of any traces of oxygen. The solution of the product will be made in a stable natural vegetable oil, which has given a negative test for vitamin D. The unit will consist of 1 mg. of the standard solution. When this dose is given daily to a rachitic rat for eight successive days, it produces a wide line of calcification in the metaphysis of the proximal end of the tibia and of the distal end of the radius.

(3) *Northern Rhodesia Copper Mines*.—An investigation lasting two months was undertaken by Dr. Ordman in connection with the occurrence of pneumonia in the native labourers on the various mines in the Northern Rhodesia copper belt. The investigation commenced in May, and included an intimate study of the various conditions which might have reference to the comparatively high incidence and mortality rates in pneumonia. The climatic circumstances, susceptibility to lung diseases of the different native tribes employed, conditions of native labour as regards surface and underground work, diet, feeding and compound housing arrangements were all examined in their possible bearing on the respiratory diseases incidence. The various hospitals were visited and all cases of respiratory disease clinically studied. Statistical data relating to disease incidence on these mines were analysed and deductions made therefrom as regards the epidemiology of pneumonia and allied conditions. An enquiry was instituted into the bacteriology of acute respiratory diseases in the native labourers of the copperfields, and finally a comprehensive report was presented.

From an epidemiological point of view the findings were of considerable interest. For, among the many cases of pneumonia studied bacteriologically, the pneumococcus was isolated in only two instances. It was found that the *Streptococcus pyogenes* was the organism primarily responsible for the respiratory infection. Other bacteria associated therewith to a lesser degree were the hæmolytic *Staphylococcus aureus*, the *Streptococcus salivarius* and the *M. catarrhalis*. A very unusual feature also was the complete absence of the *B. influenzae*, an organism which, in our experience of these investigations, is commonly found in acute respiratory disease.

A number of suggestions and recommendations were made with the object of diminishing the predisposing causes of pneumonia. As a result of the bacteriological examination a mixed vaccine containing representative strains of the organisms isolated was prepared for use as a prophylactic agent on the copper mines.

DEPARTMENT OF ENTOMOLOGY

From the 5th November, 1930, to the 16th May, 1931, Mr. De Meillon was attached to a special commission, headed by Professor Swellengrebel, investigating malaria in the Union. One of the facts brought to light, as a result of this work, was that the principle of 'species sanitation' could be applied in South Africa. The resulting widespread interest taken in this aspect of malaria control was very well reflected in the large number of larvæ and adults of anophelines sent in for identification.

In a more extended report to the Union Government on the results of his investigation, Professor Swellengrebel recommended that a field station for malaria be established by the Institute. A site was selected at Tzaneen, in the north-east, where a laboratory was suitably equipped. The Entomological Department

**THE PUBLIC HEALTH
PUNJAB DURING
-COLONEL C. A.
I.M.S. PRINTED
GOVERNMENT
RS. 44.**

to be submitted by
Punjab for over
the epidemiology of
are well known
outside India, but his
getting into being the
public health service in one
India may not be so well
the Government of the
on this report, we would like

to record an appreciation of Colonel Gill's efforts to advance the cause of public health in the Punjab.

Colonel Gill is a Neo-Sydenhamist and his remarks on the relationship of weather and economic conditions to disease are of interest. The meteorological conditions in 1931 in the Punjab were unfavourable both to epidemic plague and epidemic malaria. During the first half of the year, relative humidity was low, and rainfall was deficient, and in the second half the monsoon was normal, with no excessive rainfall in July and August. The former conditions are inimical to plague epidemics, and the latter negative the occurrence of a widespread epidemic of malaria.

The price of staple food grains continued to be low, the main cause being the decline in the export of wheat owing to the world-wide depression of trade. High prices of staple foods have in previous reports been commented on as having an adverse effect on public health, and as Colonel Gill says, it seems paradoxical to be anxious about low prices in the same connection. As a matter of fact there has been (as yet at any rate) no evidence that the peasant of the Punjab has suffered in his health from the present economic depression. As long as there is some reserve to fall back on, low food prices enable the peasant to get at least sufficient for his immediate needs.

The birth rate in the Punjab in 1931 was high, the death rate and the infantile mortality low. The rates for these calculated on the figures for 1931 were 42.7 and 26 per 1,000 of the population and 178.26 per 1,000 births respectively. The 1931 population was 23,460,267 which is 2,942,661 in excess of the 1921 population. Muhammadans increased by 14.76 per cent. in the decade, Hindus by 6.37 per cent. and Christians by 22.49 per cent. The rural population in 1931 was 86.7 per cent. of the total, as compared with 89.8 per cent. in 1921. The tendency in the decade therefore has been definitely towards urbanization.

As regards mortality, the lowest rates are in April and August and the highest in November and December. In this report 1931 followed the usual features.

Females in the Punjab up to the age of 10 have a lower death rate than males, but after this at all ages they have very definitely higher death rates than males. This is true of all the religious classes of the community. Of the chief diseases, cholera caused only 391 deaths and 706 seizures; for 4 years now the Punjab has been unusually free from cholera, but similar periods of freedom have occurred many times in the past. Such cholera as there was showed a predilection for towns, with no explosive outbreaks. Colonel Gill is of opinion that such protracted epidemics are not water-borne but due to flies and to the insanitary conditions that exist in practically all the Punjab towns. Conservancy arrangements must be improved in towns before these can hope to escape constant liability to cholera which, under present conditions, will defy all attempts at control.

Smallpox caused 3,646 deaths; there has been a steady decline in smallpox during the last few years (the present year 1932-33 has seen a distinct recrudescence however). Colonel Gill notes that there has been a hopeful increase of vaccinations especially primary. Special propaganda is necessary to reach the female population which suffers from smallpox heavily in proportion to the male population.

Plague as mentioned above was mild and confined to three districts only. It persisted in a small number of localities in the submontane tract. Colonel Gill states that there are good grounds for the opinion that plague is definitely a back number in the Punjab, but as the chart of yearly mortality shows, he is apprehensive that it may rear up its head again at any moment. He advocates continued vigilance and energy in rat destruction, though he admits that in the neighbouring Indian States, where no rat campaigns are carried out, the decline in plague has been very similar to that of the Punjab.

Malaria also was not epidemic. The solution of the problem of epidemic malaria in the Punjab lies in measures designed to prevent prolonged flooding of low-lying tracts. This has been done in parts of Lahore with marked success. The Water-logging Board is carrying out similar work wherever it is possible and has issued a set of rules and principles to be followed in the construction of canals, roads, and railways. The responsibility for urban malaria lies with municipalities, who however do not utilize the powers they have, to do much about it.

Phthisis is a scourge in the cities, though there is some uncertainty about the exact extent of its ravages. Municipalities can do something by remedying gross defects of conservancy and drainage, but the real house problem is probably a little beyond them.

Diphtheria was commoner than usual. Passive immunization was largely used in Rawalpindi, but active immunization has not yet been tried.

Leprosy is prevalent in certain areas, especially Kangra district. A special Leprosy Officer has been appointed and has done excellent work in the survey-treatment-propaganda principle advocated and carried out by Dr. Muir in various other provinces.

In the all-important matters of rural sanitation the Rural Sanitary Board gave free financial assistance for the purpose of increasing water supplies in villages located in waterless tracts; and in connection with Maternity and Child Welfare Work District Boards were given assistance to enable maternity and child welfare centres to be opened and village *daïs* to be trained. An important memorandum was drawn up setting forth the principles that should be followed in village development in the selection of village sites, layouts, water supplies, drainage and house hygiene and these are being followed in the Nili Bar Colony.

In connection with religious fairs, the interesting statement is made that incineration of night-soil is now replacing trenching. To those who have experienced the difficulties of incineration of night-soil even under disciplined conditions, this comes as rather a surprise and a description of the methods and organization would be very helpful. The activities of the Public Health Staff, the Vaccine Institute, the Epidemiological Bureau, the Chemical Laboratory, the Equipment Depot, the Educational Bureau and Health Propaganda section, are interestingly summarized. In his concluding paragraphs Colonel Gill modestly claims a share for his department for the conditions of good health pertaining during the year. In this we thoroughly agree and would again congratulate the Public Health Department of the Punjab on its alertness and activity. We wish the Director of Public Health every success in his continuation of the work of Colonel Gill.

ANNUAL REPORT ON THE MEDICAL INSPECTION OF SCHOOL CHILDREN OF THE PESHAWAR, BANNU AND DERA ISMAIL KHAN MUNICIPALITIES OF THE NORTH-WEST FRONTIER PROVINCE FOR THE YEAR ENDING JUNE 1931. PRINTED BY THE GOVERNMENT OF THE NORTH-WEST FRONTIER PROVINCE.

This report is an account of extensive and valuable work both from the point of view of immediate prevention and cure of disease as well as by the education of large numbers of children and through them their parents in elementary health matters.

The scheme of medical inspection of school children was extended to embrace all classes, *viz.* primary, middle and senior. The number of boys who were medically examined was 10,610, and the annual expenditure per boy was Re. 0-10-6. This sum is very small in comparison with the benefit received, especially when medicines were supplied to schools at a distance from hospitals; while in addition spectacles were supplied to poor children and dentists were paid merely for the intrinsic value of the work done for such children.

In Peshawar 12,462 examinations were carried out as against 6,144 during the previous year. Every boy was thoroughly examined once in every quarter.

During the first quarter of the school year 65 per cent. of the boys were examined for treatment. This percentage fell to 29 in the last quarter. The reason for this is that in the first quarter there was an influx of new students, a large number of whom came from villages. These newcomers' principal maladies were, bad eyesight, bad teeth and enlarged spleens with anæmia. All these boys had to be taught how to keep themselves clean.

It is gratifying to note that parents are more favourably inclined towards medical inspection of their children. In my last report I mentioned that one of the great difficulties in the initiation of the scheme was their total lack of interest and in fact, in some cases, open resentment against the medical authorities for even suggesting that their children needed treatment.

Medical Inspectors visited the houses of delinquent parents and explained to them why treatment of children is necessary.

'Bringing up the parent' seems to be almost more important in this Province than 'Bringing up the child'.

In the last report it was pointed out that difficulty was experienced in getting boys to attend hospital for treatment in places where schools were situated at a distance from dispensaries. This difficulty has been surmounted by supplying ordinary medicines to such schools. The medicines are in the charge of the Head Masters who give them, on the recommendation of the Medical Officer, to boys in need of them. The serious cases, however, and those requiring special medicines have still to go to the nearest hospital for treatment.

Medical Officers give lectures to every class once a quarter on hygiene, simple methods of prophylaxis of diseases, physical culture and general ideas of keeping the body and mind fit.

Uncleanliness and skin diseases.—In the first quarter 0.3 per cent. of children were found suffering from skin diseases, while in the fourth quarter only 0.2 per cent. were so suffering.

Twenty per cent. were found unclean in the first quarter as against 35 per cent. in the corresponding quarter of the last year. As a result of co-operation on the part of the school teacher, this percentage fell to seven per cent. in the last quarter.

For the purpose of combating uncleanliness separate registers are maintained by teachers who award class marks daily for cleanliness.

Dental diseases.—Twenty-four per cent. of the children examined during the last quarter required dental treatment as compared with 29 per cent. during the same quarter of the last year. This percentage includes caries of the teeth and pyorrhœa. In Peshawar 17.66 per cent. of the children suffered from dental diseases, caries 16.06 per cent., pyorrhœa 0.92 per cent., and tartar 0.68 per cent. Extractions were dealt with in hospitals but other cases were treated by private local dentists who, in a large number of cases, operated free of charge.

Affections of the ear, nose and throat, excluding enlarged tonsils and adenoids.—4.8 per cent. of the children suffered from diseases of the ear, nose and throat in the first quarter as compared with 7.5 per cent. in the same quarter of the last year. This percentage fell to 1.5 per cent. in the fourth quarter.

Enlarged tonsils and adenoids.—36.9 per cent. of the children were suffering from enlarged tonsils and adenoids in the first quarter, while in the fourth quarter this percentage was reduced to 6.6 per cent. After great persuasion 26 cases submitted to operative treatment.

The marked reduction in the percentage of sore-throats is due to the fact that children were not allowed to eat sour things, such as tamarind (*imlee*), etc. Local vendors were forbidden to sell such eatables in the schools' compounds.

External eye diseases.—Twenty-eight per cent. of the boys examined during the first quarter were suffering from external eye diseases, while in the fourth quarter this percentage fell to 5.9. This is very encouraging. The majority of these cases suffered from active trachoma.

Defective vision.—4.2 per cent. of children were found on examination to be suffering from defective vision. All these cases were corrected with spectacles excepting those suffering from diseases which would not improve even with glasses. Although there used to be great opposition to the use by children of spectacles, the parents, seeing the advantage, do not now object.

In Peshawar Municipal Schools the causes of defective vision were:—

Hypermetropia, astigmatism and myopia 4.21 per cent.; trachoma 0.54 per cent.; cataract 0.05 per cent.; corneal opacity 0.41 per cent.; and other diseases of the eye 0.03 per cent. Total defective vision in this area was 5.24 per cent.

Malaria, enlarged spleen and anaemia.—Malaria is present amongst all school children in the North-West Frontier Province. In the first quarter anaemia due to malaria was 16.23 per cent. and to enlarged spleen 7.5 per cent. while in the fourth quarter these percentages fell to 1.5 and 6.5 per cent. respectively. Last year the percentage of enlarged spleen was 11.4 per cent.

Heights, weights, chest measurements and general statement concerning the physical fitness.—A statement concerning the physical fitness of Bannu and Dera Ismail Khan school-boys of all ages, together with a comparative statement containing similar information for English boys of the same ages, is attached. The English school averages have been taken from *Lyons Medical Jurisprudence for India* by L. A. Waddell; they are for boys only. At six years of age the average height of the English school child is 3 feet 8 inches and that of the Frontier child is 3 feet 6.6 inches. The average weight of the English school child at this age is three stones and two and a half pounds and that of the Frontier child is two stones and 8.8 lbs., i.e., 7.7 lbs. lighter.

The Frontier boy at the age of six has a chest measurement in expiration of 20.8 inches and in inspiration of 22.3 inches.

At the age of six 7 per cent. of boys are of good physique and 90 per cent. of fair physique.

Vaccination against smallpox.—During the year under report 20 boys required vaccination. All of these were vaccinated.

Infectious diseases.—There was no epidemic of any infectious disease. One student in Dera Ismail Khan contracted measles.

Tuberculosis.—The following numbers of cases suffering from tuberculosis of various types were found during the year:—

(1) Pulmonary tuberculosis	3
(2) Tuberculous glands in neck	9
(3) Tuberculous sinus, foot	1
(4) Tabes mesenterica	2
(5) Cold abscess, chest	1
(6) Tuberculous sinus, neck	1
(7) Tuberculous spine	1

TOTAL .. 18

Open air classes.—The majority of school classes are regularly held outside the schools when the weather permits. Last year's remarks regarding the necessity to impart drill instruction to all primary schools do not seem to have had the desired effect as yet.

Lists of defective children.—Duplicate lists of defective children were prepared. One copy was given to the class teacher to enable him to see that the children attend hospital for treatment.

Health charts.—Class teachers conduct quarterly examinations of children for height, weight and chest measurements. The results are charted in each classroom. Diseases and defects of each child are also noted

against their names on these charts. This system creates not only a spirit of competition amongst the school children but also insures that the teaching staff takes adequate interest in the work.

Desks for primary classes.—Small desks, as recommended in the last annual report, have not been provided for the primary classes of any school. The boys still squat on the floor and this leads to bad postures.

School buildings.—It is regretted that it has not been possible as yet to do anything for the Islamia High School, Peshawar City. In the last annual report the building was condemned as being unfit for school premises. It is insanitary, dark, and in a dilapidated state. It is altogether unsuited to house children for six hours a day.

The remarks in the last reports about the Sanatan Dharam High School, Peshawar City, and the Khalsa Middle School, Peshawar Cantonment, still hold good. Both buildings are in a bad state of repair. They are dark, damp, congested, with low ceilings, and altogether unsuited for schools.

It is gratifying to note that the Municipal Board Primary School, Jahangirpura, Peshawar City, has acquired a new building.

New pucca latrines have been built in the Mission High School, Peshawar City.

The primary school latrines are insanitary and more supervision is necessary.

Both the Sanatan Dharam School and the Islamia Primary School in Bannu require re-building. Last year it was understood that both of these schools intended to acquire new buildings, but nothing appears to have been done so far.

Dera Ismail Khan.—Both the Islamia Branch No. 1 and the Vedic Primary School buildings are still bad, being ill-ventilated and dark.

General remarks.—Thirty-six surgical operations were performed on school children; these included twenty-six operations on enlarged tonsils, and five on tuberculous glands in the neck. There is still, however, great difficulty being experienced in securing the parents' consent to operative treatment for their children. This difficulty, which was the cause of no operations having been performed last year, has, as a result of a distinct improvement in the parents' attitude towards surgical treatment, been partially surmounted.

Special mention is made of the work done by Dr. Camphor, Dental Surgeon, Peshawar, in Peshawar City. He has done excellent work and has, in fact, refused payment even for the intrinsic value of work done by him. This resulted in a saving of Rs. 190 to Government. He has also volunteered to attend all the poor boys free of charge for so long as the present financial situation lasts.

On recent reports on school work in England, great stress has been laid on the importance of food in determining the health and physique of scholars and on the need for a mid-day meal. In India the Indian school boy has his first meal at 8-30 A.M. and then has nothing until about 6 P.M. This period is far too long and is definitely bad for the growing boy. In the recess in the middle of the morning he is hungry and, instead of having suitable food, he buys sweetmeats from the local vendor which are deleterious to his health.

It is proposed as an experimental measure to introduce a mid-day meal in the Khalsa High School, Peshawar City. If this be a success the measure will be extended to all schools in the Municipality. The cost per head will be about only Rs. 2 per mensem, and it is hoped that this small amount will not be grudged by the parents. This meal will be prepared at the schools.

ANNUAL REPORT OF THE EUROPEAN AND INDIAN MENTAL HOSPITALS, RANCHI, FOR 1931.

The reports of both these institutions for the year 1930 have been reviewed by us at length in our issue of January this year and as the greater part of these reports is very similar from year to year we propose

to deal with them quite briefly on this occasion. The table below gives the comparative total figures for 1930 and 1931, which show little change.

TABLE
Average daily strength

	Year	Males	Females	Total
European hospital	1930	99.90	100.71	200.61
	1931	97.82	98.59	196.41
Indian hospital	1930	1,010.05	218.08	1,258.13
	1931	1,033.34	226.07	1,259.41

In respect of the European hospital, however, one new, and we think original, form of treatment has been introduced by Lieutenant-Colonel Berkeley-Hill. This is in the form of a creed which is taught to the patients and is perhaps best explained by quoting from the report in full.

Introduction of a new feature in the form of a Creed.—A new feature in the form of a Creed was introduced during the year under review. The idea of this Creed is to re-assure patients, especially new patients, of the desire on the part of every member of the staff to devote his (or her) energy towards procuring the patients' recovery.

'The care of the Human Mind is the Noblest Branch of Medicine.'—Grotius.

CREED

'We believe in a healthy mind, in a healthy body, and we are co-operating with the doctors, nurses and the occupational therapists of the Ranchi European Mental Hospital to this end.

We recognize the goodwill and sincere interest of the Board of Trustees in the various measures ordered to restore us to health, and thus to useful and happy lives in our respective communities. We believe mental illness to be a honourable affliction, and we take pride in our efforts to regain mental and emotional vigour.

We look with undying hope towards the future, with faith in ourselves and with confidence in those appointed to assist us towards recovery. With goodwill towards all, we believe that this is a wonderful world, once we understand it. Even happier days are ahead'.

It is of course too early to form an opinion as to the value of this method.

ABSTRACTED FROM THE ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, FOR THE YEAR ENDING 31ST DECEMBER, 1931.

THE number of patients treated at the institute during the year was 545, an increase of 4 as compared with the figure for the previous year. Out of the 545 treated, 7 died from hydrophobia, a mortality rate of 1.28 per cent. At the close of the year 28 patients remained under treatment.

Advice is occasionally sought on the question whether treatment is necessary in the case of persons who have drunk the milk or have eaten the meat of animals suspected to be rabid. If the milk has been boiled and the meat cooked before use, treatment is not advised.

Simple's carbolized sheep vaccine was in use throughout the year. No marked reaction was noted in any of the cases treated with 5 per cent vaccine. No complications of any sort, nor any paralytic accidents have followed the treatment.

Antirabic vaccine for treating 9,325 persons was issued to the centres during the year under report. Of these, 8,056 are reported to have received a complete course of treatment; and there were 60 deaths among

them, a mortality rate of 0.74 per cent. Of the 60 who died, 2 were Europeans and the rest were Asiatics.

Out of the 8,601 cases treated at the institute and at the centres during the year, 8,130 were dog bites, 189 were jackal bites and 42 were fox bites.

Jackal bites account for nine out of the sixty-seven deaths. Fox bite accounts for one death and the remaining fifty-seven deaths are all from dog bites.

In three cases, the incubation period was very short, 16 days in one case treated at Tanjore, 16 days in another treated at Mangalore and 17 days in the third treated at Madura; all these three deaths were from dog bites.

In three other instances, the incubation period was very long, 247 days in a case of jackal bite treated at Cocanada, 222 days in a case of dog bite (European) treated at Lallaguda and 190 days in another case of dog bite treated at Salem.

The mortality from hydrophobia in the rural areas of the Presidency continues to be high and the figure for 1931 is higher than that in any of the preceding years. Though the antirabic treatment is decentralized to a very great extent in this Presidency, still persons in rural areas are not aware of the treatment given in Head-quarter Hospitals. More intensive propaganda work in the rural areas on the value of antirabic treatment is being carried out. The demand for vaccine is steadily on the increase. Training in the technique of antirabic treatment was given to 30 government medical officers and also to 14 medical officers from Native States and railways during the year 1931.

Three hundred and seventeen brains of rabid or suspected-rabid animals were sent to this institute for examination, by veterinary surgeons in the Presidency and Native States. We believe this figure could be much larger if veterinary surgeons would pay special attention to this important line of work.

During the past years, we have, in addition to antirabic work, undertaken to help the hospitals and medical practitioners in the Nilgiris District by doing their clinical and bacteriological work. We believe this work is being more and more appreciated by those who send their specimens to us for examination. The figures for 1931 are an increase on those of 1930.

During the past few years many improvements have been carried out at the institute. The institute is now provided with a very fine set of animal rooms where rabbits, guinea-pigs and pigeons are kept under perfect sanitary conditions. Runs have been erected for these animals to live under natural conditions. As a result of breeding under such healthy conditions, our stock throughout the year has been a healthy one and we have been able to supply other institutions with animals. During the year 1931, we supplied a large number of rabbits and guinea-pigs to various places from our surplus stock. Accommodation for sheep has also been provided, but this will have to be increased in the next year owing to the exclusive use of sheep for the preparation of antirabic vaccine and also on account of the higher dosage treatment being introduced.

In the year 1930, a cold chamber 'Hall's Patent' was erected at a cost of Rs. 10,733 and the work was carried out by Messrs. Marshall and Sons, Ltd., Madras. It was brought into use during the year under review.

Correspondence

INDIAN MALE NURSES

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I would like to bring to your notice the question of the employment of trained Indian male nurses in government and other hospitals.

Our C. M. S. Men's Hospitals (in Peshawar, Burma, D. I. Khan, and Quetta) are now training-schools for male nurses. We give selected boys solid teaching in anatomy, hygiene, and nursing (theoretical and

practical) for three years, and after each year they have to pass an examination set by the North Indian United Board of Examiners from mission and other hospitals.

These papers are not easy and the standard for pass marks tends always to get higher.

Our aim is to turn out boys fully qualified to be nurses and I think we may say that in this we have succeeded. Should they wish to qualify as 'compounders' they must take another course extending to two years, with an examination at the end of each year set by the same Board. Should they be successful, another certificate is then issued to them.

We feel that those thus equipped and who have certificated in both nursing and compounding are safe to be set free to make their own living, whether in private practice or in institutions, and instead of being a danger to their fellow-countrymen can serve them safely and efficiently.

But the difficulty is to get them employment after they are qualified. The military hospitals will not take them unless they start at the bottom of their ladders, and so far civil hospitals have not seen their way to take them, as the civil authorities say they prefer to take their own men.

We are very anxious that you should recognize our certificates and employ our boys as fully-qualified nurses and compounders, giving them the pay to which they are entitled as such.

We feel we are doing a real service for India in training male nurses and compounders and it would be disastrous if their training were to cease; but cease it must, unless we can obtain employment for those already trained.

Government and other hospitals may be glad to hear of these male nurses trained at our mission hospitals and I should be delighted to recommend several who are looking for employment.

Yours, etc.,

H. T. HOLLAND, M.B., B.S. (U. Edin.),
F.R.C.S. (Edin.).

C. M. S. HOSPITAL,
QUETTA,
16th March, 1933.

THE TREATMENT OF ACNE

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I shall be glad if you will publish the following in the next issue of the *Gazette*:—

A friend of mine has suffered from acne vulgaris for two years. Though many remedies have been employed, none has effected a cure, and so the acne and the ugly scars caused thereby still prevail. Will some member of my profession be kind enough to suggest a remedy for the removal of the acne and scars.

Yours, etc.,

P. H. BHATT, D.A.M. (Baroda Government).

LOKOPYOGI DISPENSARY,
DOLARANA'S VASNA (MAHIKATHA),
23rd February, 1933.

[Note.—This letter was submitted to Lieutenant-Colonel H. W. Acton, C.I.E., I.M.S., Director of the Calcutta School of Tropical Medicine, who has given us the following note:—

The treatment for acne vulgaris consists in the proper removal of the scales and plugs from the sebaceous-gland mouths. This can be done by the use of plenty of soap and hot water, or by using ether soap consisting of one part ether, one part alcohol and one part soft green soap. A lotion consisting of lotio alba, zinci sulphas and potassa sulphurata, 20 grains each in an ounce of water, should be lightly dabbed on to the face and, when dry, rubbed into the skin by the fingers. The lotion should at first be used twice a day and then

once, sufficient to produce hyperæmia and desquamation of the cheek. If the reaction is excessive a little cold cream can be put on at night. The scalp should also be attended to for seborrhœa.—EDITOR, I. M. G.]

COMPARATIVE NOTES ON THE CRYOSCOPY OF MILK

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—With reference to my paper entitled 'Comparative Notes on the Cryoscopy of Milk' which appeared in the *Indian Medical Gazette* of January 1933, I have had a number of enquiries as to the exact significance of the cryoscopic determination when applied to the adulteration of milk in the tropics. This question has already been answered in a paper published from this laboratory in the *Analyst*, 1932, LVII, 449. As a result of systematic study of a large number of samples of both cow's and buffalo's milk, from herds and from individual animals, over a period of eleven months (April 1930 to March 1931), it is shown that wherever possible cryoscopic examination of the milk supply is of the utmost importance, since the addition of water to buffalo's milk, so that the lower standards for cow's milk (i.e., for fat and solids-not-fat) are complied with, cannot escape detection, if the freezing point of the sample is investigated.

Subsequent experience has emphasized the importance of the method and its utility in meeting the many difficulties of a dual milk supply that arise in the East.

I would also bring to your notice that in the original typescript of my article 'Observations on the Composition of Butter Imported into Burma', published in your issue of June 1932, a typing error escaped my notice. The word 'importing' should read 'exporting' in the second line. The error is fairly obvious from the other descriptive details given.

Yours, etc.,

E. H. BUNCE, F.I.C., F.C.S.,
Public Analyst to the Government of Burma.

HARCOURT BUTLER INSTITUTE
OF PUBLIC HEALTH, RANGOON,
15th March, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

BREVET-COLONEL H. H. THORBURN, C.I.E., an Agency Surgeon, is posted as Civil Surgeon, Ajmer, and Chief Medical Officer, Rajputana, with effect from the forenoon of the 17th February, 1933.

Brevet-Colonel C. A. Gill, R.A.S., Officiating Inspector-General of Civil Hospitals, Burma, is confirmed in that post, with effect from the 18th February, 1933.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff, with effect from the 28th February, 1933:—Lieutenant-Colonel A. H. Proctor, D.S.O., M.S., to be Honorary Surgeon, vice Major-General C. A. Sprawson, C.I.E., tenure expired.

Lieutenant-Colonel H. E. Stanger-Leathes is appointed Honorary Surgeon to The King, and promoted Brevet-Colonel, vice Major-General C. Hudson, C.B., C.I.E., D.S.O., 24th September, 1932.

Lieutenant-Colonel A. H. Proctor, D.S.O., Surgeon-Superintendent, Presidency General Hospital, Calcutta, is appointed to officiate as Surgeon-General with the Government of Bengal during the period of the leave granted to Major-General W. V. Coppinger.

Lieutenant-Colonel R. H. Candy, Civil Surgeon, Ahmedabad, to be Civil Surgeon, Poona, with attached duties, vice Major S. R. Prall, proceeding on leave.

Lieutenant-Colonel W. C. Spackman to officiate as Superintendent, J. J. Hospital, Bombay, in addition to his own duties.

Major H. E. Murray is appointed to act as Surgeon-Superintendent, Presidency General Hospital, Calcutta, with effect from the date he takes over charge, *vice* Lieutenant-Colonel A. H. Proctor.

Major W. H. Crichton is appointed substantively to be an Agency Surgeon, under the Government of India in the Foreign and Political Department, with effect from the 5th February, 1933.

Major B. G. Mallya is appointed until further orders to act as Superintendent, Campbell Medical School and Hospital, Calcutta, with effect from the date he takes over charge, *vice* Major S. N. Mukherji, granted leave.

The services of Major G. Verghese are placed temporarily at the disposal of the Government of Bihar and Orissa, for employment in the Jail Department, with effect from the date that he assumes charge of his duties.

Major J. Rodger, M.C., Civil Surgeon, Sibi, is appointed temporarily to officiate as Residency Surgeon and Chief Medical Officer in Baluchistan, in addition to his own duties, with effect from the afternoon of the 13th February, 1933, and until further orders.

Major H. Williamson, M.B., on return from leave resumed charge of the duties of the Civil Surgeon, Quetta, with effect from the forenoon of the 16th February, 1933.

Major F. R. Thornton, M.C., Officiating Civil Surgeon, Nasik, to be Civil Surgeon, Ahmedabad, with attached duties, *vice* Lieutenant-Colonel R. H. Candy.

The services of Captain H. D. R. Zscherpel are placed at the disposal of the Government of North-West Frontier Province, for employment in the Jail Department, with effect from the date on which he assumes charge of his duties.

The undermentioned appointments are made:—

To be Captains (on probn.)

W. J. Mody, 1st February, 1933, with seniority 6th December, 1932.

A. E. Kingston, 1st February, 1933.

To be Lieutenants (on probn.)

1st February, 1933, with seniority 1st February, 1932

J. D. Murdoch.

G. B. Thomas.

A. T. Andreasen.

1st February, 1933

J. M. Selater.

D. R. Tweedie.

C. F. Garfit.

J. W. Richmond.

G. S. N. Hughes.

A. D. Barber.

David Kenneth Llewelyn Lindsay, 1st February, 1933, with seniority 1st February, 1932.

LEAVE

Major-General W. C. H. Forster, C.I.E., V.H.S., Surgeon-General with the Government of Bombay, is granted, preparatory to retirement, leave on average pay for 2 months and 24 days followed by leave on half average pay for 28 days, with effect from the 28th March, 1933.

Major-General W. V. Coppinger, C.I.E., D.S.O., Surgeon-General with the Government of Bengal, is granted combined leave for 8 months, with effect from the 15th March, 1933, or subsequent date from which he may avail himself of it.

Lieutenant-Colonel H. W. Acton, C.I.E., Director and Professor of Bacteriology and Pathology, School of Tropical Medicine, Calcutta, is allowed leave on average pay for the period from the 8th April to the 15th April, 1933, and from the 15th July, 1933, to the 18th November, 1933, sandwiching the summer vacation of the School of Tropical Medicine, Calcutta, for the year 1933 for the period from the 16th April to the 14th July, 1933.

Lieutenant-Colonel T. C. Boyd, Principal, Medical College, and Superintendent, Medical College Hospitals,

Calcutta, is allowed leave for the period from the 6th April to the 22nd July, 1933.

Lieutenant-Colonel S. S. Vazifdar, Professor of Medicine and Clinical Medicine, Grant Medical College, and Physician and Superintendent, J. J. Hospital, Bombay, is granted leave for 8 months out of India, with effect from 13th March, 1933, or the date of availing.

Major S. N. Mukherji, Superintendent, Campbell Medical School and Hospital, Calcutta, is allowed leave for 8 months out of India or Ceylon, with effect from the 9th March, 1933, or the date of availing.

Major S. R. Prall, Officiating Civil Surgeon and Superintendent, B. J. Medical School, Poona, is granted leave for 4 months combined with furlough for 8 months, with effect from the 1st April, 1933, or subsequent date of availing.

PROMOTIONS

Captain (provl.) (on probn.) to be Major (provl.) (on probn.)

W. Aitchinson, M.C. Dated 20th December, 1932.

Lieutenants to be Captains

S. M. Kharegat. Dated 15th July, 1932.

R. C. Dracup. Dated 6th November, 1932.

Lieutenants (on probn.) to be Captains (on probn.)

A. K. Gupta. Dated 15th July, 1931.

Hoe Min Sein. Dated 26th January, 1933.

Note.—The provisional promotion of the undermentioned officers to the rank of Captain is confirmed:—

Captain (provl.) (on probn.) J. Singh.

Captain (provl.) (on probn.) K. Jilani.

Lieutenants to be Captains (provl.)

A. B. Guild. Dated 4th February, 1933.

A. W. West. Dated 3rd February, 1933.

RETIREMENTS

Colonel W. H. Leonard, K.H.P. Dated 12th February, 1933.

Lieutenant-Colonel J. F. Boyd. Dated 31st January, 1933.

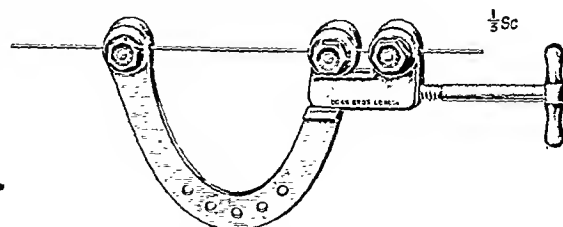
Notes

MODIFICATION OF KIRSCHNER'S STIRRUP

By N. A. KINNEAR, M.B., B.Ch.

This modification of Kirschner's stirrup, for use in his system of piano-wire extension of fractures, seems to have advantages over some other types of stirrup.

The threading of the wire through the stirrup is simple. It is impossible to twist, and so fracture, the wire while tightening it. After the wire has been tightened it is securely and rigidly held in the stirrup by the end-piece locknuts. The stretcher is detachable and only one is necessary for any size or number of stirrups, expense being thus reduced.



There are two alternative sizes of end-piece nuts and five sizes of stirrup to suit the olecranon, the tibial tubercle, the calcaneum, or the lower end of the femur. In practice, I think, it will be found that two sizes of stirrup will be sufficient.

The instrument is reasonably priced and has been made for me by Messrs. Down Bros.

RADIOSTOL AND RADIOSTOLEUM

RADIOSTOL

RADIOSTOL is the original British irradiated ergosterol; it was issued for medical use in February 1927.

Until Radiostol was made available for medical use, the population of the world depended for its requirements of vitamin D upon the intake of the vitamin through the medium of food and upon the action of the sun's rays on the skin—the presence of minute traces of ergosterol in the skin of human beings and of animals making this natural method of production possible. The supply of vitamin D, therefore, was often inadequate and always uncertain; hence the production of Radiostol by the action of ultraviolet light upon ergosterol, with the consequent availability of a supply of vitamin D more than sufficient to cover all requirements, is of paramount importance in the maintenance of health, particularly in early life.

Radiostol, in the form of solution or pellets, is vitamin D standardized and exhibited for use in medicine; in fact from the time of its first issue Radiostol has been manufactured under scientific control, and its vitamin-D activity has been maintained at a definite standard.

The unitage adopted for expressing the activity of Radiostol is that described by the Medical Research Council, London. Radiostol is standardized in terms of the standard preparation of irradiated ergosterol issued by the Medical Research Council which contains 1,000 units vitamin-D activity per c.cm. This standard has been adopted recently for international use by the Permanent Standards Commission of the Health Organization of the League of Nations (*see p. 295*). Thus the potency of Radiostol is already expressed in terms of the International Standard. The tests are carried out on rats made rachitic by being fed on appropriate diet; the criterion used is the deposition of calcium in the cartilage at the proximal end of the tibia and the distal ends of the radius and ulna (the 'line' test).

The normal function of vitamin D is to control calcium and phosphorus metabolism, and it is now established that correct calcium and phosphorus metabolism is possible only when the available vitamin D is adequate; any increase in the calcium and phosphorus intake has little effect upon the development of bones and teeth when there is a deficiency in the vitamin-D absorption.

RADIOSTOLEUM

Radiostoleum supplies vitamins A and D in accurately-measured quantities and in the scientifically-balanced proportions in which it has been shown by experiment, and confirmed in clinical practice, that they can be assimilated to the best advantage. The proportions in which these vitamins occur in any particular product in nature is not constant, and there is no correlation between the vitamin-A value and the vitamin-D value of the natural sources of these vitamins. It has, in fact, been shown that one sample of cod-liver oil may be rich in vitamin A, but poor in vitamin D; another may show a high vitamin-D, but a low vitamin-A, content.

The vitamin A in Radiostoleum is present as an accurately-measured portion of a purified concentrate made by a special process evolved in the B. D. H. laboratories; the vitamin D is a measured quantity of pure crystals of this vitamin.

Radiostoleum is standardized to contain vitamin A and vitamin D in the following proportions:—

Liquid—

Vitamin A : 500 blue (Carr-Price value).

Vitamin D : 3000 International units of antirachitic activity per gramme.

Capsules—

Vitamin A .. 1000 blue (Carr-Price value).

Vitamin D .. 1200 International units of antirachitic activity per capsule.

Radiostoleum is the original concentrated preparation of vitamin A and vitamin D used in medicine. In fact, Radiostoleum is the product through the medium of

which the 'anti-infective' action of vitamin A was established.

In their original experiments in the Jessop Hospital, Sheffield, Mellanby and Green found that the administration of massive doses of Radiostoleum produced distinctly beneficial effects in cases of puerperal septicaemia; later the value of Radiostoleum in the prophylaxis of puerperal septicaemia was established definitely by these same workers who, treating 275 pregnant women with Radiostoleum whilst keeping 275 as controls, found that of the women treated with Radiostoleum only 1.09 per cent. developed puerperal morbidity after delivery, whilst 4.73 per cent. of the controls became infected.

McCarrison also used Radiostoleum in his experiments in India, in which he found that by its administration it was possible to maintain the integrity of the epithelial linings of the body, particularly those of 'the respiratory passages, the urinary tract, the reproductive tract, the conjunctiva, the nasal passages, the ear, and the ducts of organs'.

Copies of a booklet describing the above products will be supplied free of charge to any member of the medical profession in India on request from one of the B. D. H. representatives whose names and addresses are as follows; Henry S. Clark & Co., 27/4, Waterloo Street, Calcutta, and Byram Mistry, 109, Parsi Bazar Street, Fort, Bombay No. 1.

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Original Articles

THE PATHOLOGY OF ELEPHANTIASIS OF FILARIAL ORIGIN

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THE term 'elephantiasis' was first used by Celsus to indicate leprosy, and later by Galen (130 to 200 A.D.) to indicate both leprosy and true elephantiasis. A third disease Madura foot was also generally confused with leprosy and elephantiasis until about the eighteenth century. In 1750, Hillary gave a full and lucid account of the evolution of the large leg of elephantiasis, wherein he clearly differentiated this disease from leprosy. The classical researches of Danielssen and Boeck in 1848 on leprosy, and those of Vandyke Carter in 1860 on mycetoma, established clearly the nature of and distinction between these three diseases. The aetiology of elephantiasis was further elucidated by the discoveries of the microfilariae by Wucherer in 1866 and Lewis in 1872, and the adult filarial worms and their abodes by Bancroft in 1876. About the same time, Manson carried out pioneer investigations in filarial infection in China. Following Fedtschenko, who first demonstrated in 1870 the rôle of cyclops as the intermediary host in the transmission of guinea-worm in man, Manson made the memorable discovery in 1878 that the mosquito was the carrier of filarial infection. By the close of the nineteenth century, while researches were being carried on to establish the true parasitic origin of the filarial diseases, the low microfilaria rate in those with elephantiasis puzzled many observers and considerable opposition was therefore raised to the acceptance of its parasitic origin.

Even in the present state of our knowledge there appears to be some confusion among the writers on the subject regarding the pathological signs of the infection, and several diseases of non-filarial origin are often included under the heading of elephantiasis. Cases of dermatolysis, hypopituitarism and vulvar growths of septic origin, which also show signs of pachydermia, are often mistaken for elephantiasis of filarial origin and are described as such. Any condition which is capable of producing obstruction of the lymphatic system may result in symptoms similar to those produced by filarial infection. The distinction between elephantiasis of filarial origin and elephantiasis nostra was not clearly recognized till recently, and it was suggested by

some investigators that the two diseases were of the same origin and that the presence of microfilariae in the peripheral blood of the former in the early stage of the disease was merely a coincidence.

Regarding the aetiology of elephantiasis of filarial origin also, we often notice among the investigators an imperfect understanding of all the factors which are responsible for the production of the disease. For instance, one or two recent workers appear to think that all the pathological conditions observed in all cases of filariasis are attributable to the presence of the parasite alone. The importance of secondary infection in the causation of filarial lymphangitis is altogether ignored. Such a view is a priori contrary to the bacteriological findings of various investigators in this field. Extensive observations made by us during the last ten years definitely show that while the worm (*Wuchereria bancrofti*) is primarily responsible in all cases for the damage to the lymphatic system, the pathological conditions in a large number of advanced cases of elephantiasis are mostly due to the secondary bacterial infection. This question was considered in detail by the authors in the paper 'Kataphylaxia in filariasis' (1929). The production of a toxin by the adult female parasite was for the first time demonstrated by these authors in the above paper. A distinct eosinophil reaction in the lymphatics was observed in the region of the anterior end of the worm where the vulva is situated, while it was not perceptible in the tail region. The authors were also the first to record cases of urticaria which were purely filarial in origin. That the liberation of this toxin was responsible for the production of allergic symptoms, such as periodic headache, migraine, and slight rise of temperature, in filarial patients was clearly recognized and was mentioned in this paper. The importance of the susceptibility factor was emphasized as being responsible for the differences in sensitiveness to the toxin in regard to allergic manifestation. A sentence from one of our previous papers (1931) may be quoted here. 'There is a definite type of lymphatic obstruction which is helminthic in origin and can be proved to be so on definite geographical, epidemiological and pathological evidence as due to *Filaria bancrofti*'. Although great stress was laid on the helminthic origin of the infection as is evident from the above, the possibility of 'superimposed septic infection as the result of a lowering of the local defence mechanism' was not overlooked.

A common mistake that is still prevalent among practitioners is to look for microfilariae in the blood in cases of elephantiasis. It is not yet generally understood that by the very nature of the infection it is not always possible to find the microfilariae in the blood, especially when elephantiasis is the result of lymphatic block by the adult worms. The microfilaria which is in a sheath is incapable of

independent movement and is carried by the normal flow of lymph to the blood stream, so that when there is obstruction of the lymphatic vessel they are not able to reach the blood, with the result that the microfilaria rate is low in cases of elephantiasis.

Another fallacious notion which is prevalent is that the œdema due to other causes can be differentiated from that due to elephantiasis by the pitting-on-pressure test. Although elephantoid skin does not pit on pressure in the later stages, such pitting on pressure does occur during the early stages of the disease, so that this diagnostic feature is misleading.

It is therefore proposed to give in this paper an account of the pathology of elephantiasis and its gradual development from the time the filarial worms live in the lymphatics without any apparent injury to the human system.

It is convenient to consider the pathology of filariasis under the two headings, (a) that due to the filarial toxin, and (b) that due to the secondary infection. The clinical symptoms and the various factors, such as individual susceptibility, intensity of infection, etc., which influence the types of lesions are discussed.

(a) DUE TO FILARIAL TOXIN

Production of signs and symptoms

A certain percentage of the population in an endemic area harbour the filarial worms for several years without apparently suffering injurious effects, or manifesting signs or symptoms of disease; these people thus act as carriers of the infection. The adult filarial worms live in the main lymphatics and in the hila

of the glands draining the extremities, and the sheathed embryos, as they are discharged by the adult female into the lymphatic vessels, are carried to the blood stream, provided there is no obstruction to their passage. In many instances, however, the adult worms and embryos are found lying on the distal side of an enlarged or fibrosed gland, so that the embryos are not able to reach the blood stream. An interesting case of this description may be recorded here :

B. S., Hindu, male, aged 35, was admitted into the Carmichael Hospital for Tropical Diseases for enlarged inguinal glands (left). Although no microfilariae were present in the blood, clinical examination pointed to a filarial infection of the inguinal glands. The glands were excised under local anaesthesia and three adult filariae actively coiling and uncoiling were found in one of them. The worms were separated out and the glands were imbedded for sectioning. Serial sections of these glands were cut and in these many more mature filariae were found in the lumina of the lymphatic vessels (*vide* figures 1 to 3). It is interesting to note that, although the worms recovered from these glands were quite mature and full of embryos, no microfilariae were demonstrable in the blood of the patient.

There have also been other patients in whose lymphatics and glands mature parasites were found and whose blood did not show microfilariae.

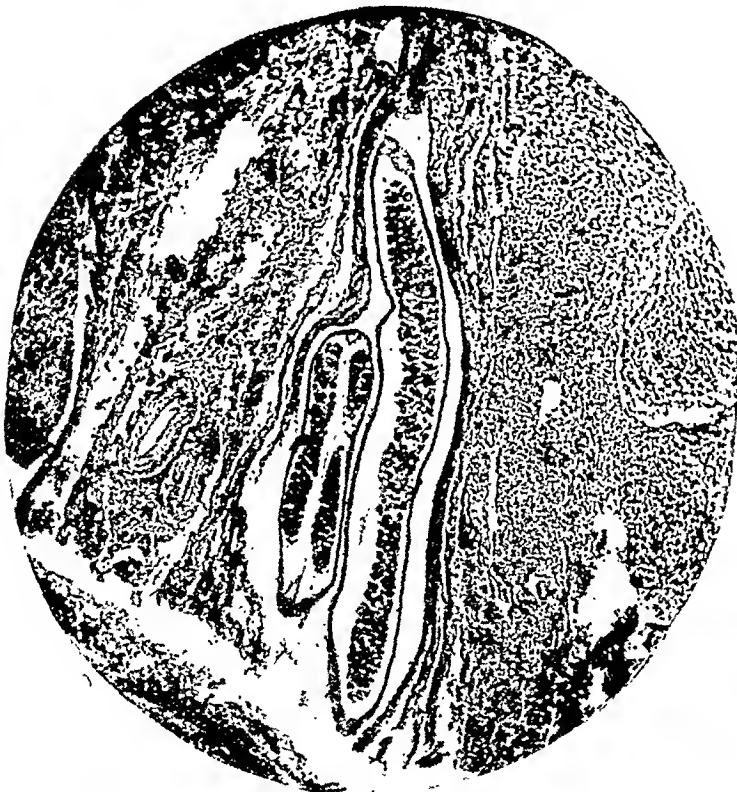


Fig. 1.—Photomicrograph of gland section showing the adult filaria.



Fig. 2.—Photomicrograph of gland section The adult filaria is seen in section.

Microfilaria rate

It is seen from the above that blood examination does not always give a true indication of

such patients for any considerable length of time. Such cases are therefore of interest as they have been under our close observation for



Fig. 3.—Photomicrograph of gland section showing adult filaria in section.

the incidence of filarial infection in a given population and yet for practical purposes the microfilaria rate may be taken as a guide to estimate the amount of filarial infection in a population. The microfilaria rate varies from area to area, and even in different wards of the same town. The factors which influence these variations will be dealt with in a later part of the paper. Table I shows the microfilaria rate among the healthy population of Calcutta. These observations are based on one single examination of a thick smear of the peripheral blood taken at midnight. We have now under our observation several persons who have shown microfilariae in their peripheral blood for the last ten years. Periodical examination of the peripheral blood taken during the night in these cases has shown the presence of embryos on every occasion but so far in none of them has there been any manifest sign or symptom of filarial disease. Several of these belong to the staff of the School of Tropical Medicine.

It may be mentioned that though filariasis is endemic in several parts in India there is so far no record of the results of observation of

TABLE I

Microfilaria rate of Calcutta city (based on a total examination of 2,922 persons from jails, hospitals, hostels and the public during 1927-1933. They include persons of all nationalities and of both sexes)

Age-period	Number examined	Number showing microfilariae	Percentage
1-5 ..	86	0	0.0
6-10 ..	78	3	3.9
11-15 ..	358	14	3.9
16-20 ..	498	21	4.2
21-25 ..	420	58	13.8
26-30 ..	403	51	12.6
31-35 ..	238	25	10.5
36-40 ..	197	22	11.2
41-45 ..	218	26	12.0
46-50 ..	221	24	7.5
51-55 ..	103	11	10.7
56-60 ..	79	9	11.4
Over 60 ..	23	1	4.4
TOTAL ..	2,922	265	9.1

TABLE II

Blood counts in 100 cases of filariasis with microfilariae in peripheral blood, showing an eosinophilia of over 5 per cent in 62 cases

Total leucocytes per c.mm.	Total eosinophils per c.mm.												
	250	500	750	1,000	1,250	1,500	1,750	2,000	2,250	2,500	2,750	3,000	
3,000	..	1	1
4,000	2	2
5,000	..	1	1
6,000	4	4	9	1	18
7,000	4	13	5	2	1	25
8,000	..	7	2	18	1	28
9,000	..	1	5	4	2	12
10,000	1	1	1	3
11,000	1	1
12,000	1	1	2
13,000	1	1	2
14,000	1	1
15,000
16,000	..	1	1	2
17,000	1	1
19,000	1	..	1
23,000
	10	28	23	29	7	1	..	1	1	..	100

TABLE III

Blood counts in 100 cases of filariasis with no microfilariae in peripheral blood, showing an eosinophilia of over 5 per cent in 20 cases

Total leucocytes per c.mm.	Total eosinophils per c.mm.												
	250	500	750	1,000	1,250	1,500	1,750	2,000	2,250	2,500	2,750	3,000	
3,000
4,000
5,000	1	1
6,000	2	3	1	6
7,000	6	10	1	1	18
8,000	3	16	3	1	23
9,000	5	14	1	1	1	1	23
10,000	2	2	5	1	1	11
11,000	2	3	1	6
12,000	1	1	1	3
13,000	1	..	1	2
14,000	1	1	2
15,000	..	2
16,000
17,000	2
20,000	..	1	..	1	1
23,000	..	1
	22	54	15	5	3	1	100

a long period. A large number of other persons in Calcutta in whom occasional blood examination has shown the infection have been living free from filarial disease for a long time. These cases are not referred to here as continuous observation for a sufficiently long period has not been possible.

Moderate eosinophilia the result of filarial toxin

From a study of the eosinophil response in filarial infections it has been found that the total eosinophils range from 400 to 800 per e.mm. A careful study of this reaction has also been made in the different stages of filarial diseases and the results are tabulated on the previous page. The total and differential counts were made in all the cases at about the same time of day. Tables II and III show the total eosinophil counts in cases of filariasis with microfilariae in blood and those without microfilariae. From the tables it will be seen that, when there is no obstruction and microfilariae are present in the blood, there is a constant high eosinophilia indicating the leakage of toxins into the peripheral blood. This question has been dealt with by us in detail in a previous communication (1929). In the early stages of filarial diseases, where there is partial obstruction, the average eosinophilia shows a distinct decrease. In elephantiasis where the lymphatic obstruction is complete there is no indication of the toxin in the blood and the eosinophil count is practically normal. In such cases the parasite is dead, and either absorbed or calcified.

Anaphylactic symptoms

In persons who harbour filarial worms anaphylactic symptoms due to filarial toxin are sometimes observed. The patients may suffer from periodical headache, migraine, urticaria, pain in the joints and muscles, small rises of temperature, 99°—99.8°F., etc. In an earlier communication cases of urticaria due to filarial toxin have been reported by us (1930). The following additional cases may be mentioned here:

B. B. M., Hindu, male, aged 37, suffering from migraine for the last 1½ years, attacks appear periodically once a fortnight or once a month; attacks last for 24 to 36 hours at a time; no fever; microfilariae present in the peripheral blood; no other focus of infection present. Total eosinophils 600 per e.mm.

X, Anglo-Indian, male, aged 12, admitted for daily rises of temperature between 99°—99.8°F. for the last two and a half months. Blood culture, Widal reaction, and stool culture—negative; microfilariae present in the peripheral blood; eosinophils 500 per e.mm.; symptoms cleared up with soamin treatment.

T. S., Hindu, male, aged 45, complained of pain in the muscles and joints including small joints of the fingers. The attacks appeared off and on for one year; no definite periodicity noted; examination of teeth, gums, throat revealed no abnormality; stool and urine examination did not show any infection. Microfilariae present in the peripheral blood. A month after the discovery of microfilariae in the blood, the dorsum of the left hand was swollen; a lymphatic cyst was opened and lymph with microfilariae in it drained from this. The blood did not show any microfilariae at this stage.

Anaphylactic symptoms are generally observed during the early stage of filarial infection in susceptible persons. In elephantiasis the obstruction is at the inguinal, the axillary or the epitrochlear region. As the main lymphatic is blocked the toxin is not able to reach the blood and allergic symptoms are therefore localized or absent. The toxin acts locally on the tissue cells and increases their permeability with the result that static oedema develops.

Dermal tests as evidence of toxin

Several attempts have been made in recent years to evolve a satisfactory dermal test to detect filarial infection in the human system. Owing to the difficulty of obtaining adult worms it has not been possible till now to carry out these tests with the *Wuchereria bancrofti* antigen. The tests are therefore carried out with the antigen of allied species. Taliaferro and Hoffman (1930) and Hamilton Fairley (1931) have reported promising results with *Dirofilaria immitis* antigen. With a view to diagnosing the presence of filarial infection, the above tests were carried out on a number of persons in our laboratories. In our earlier experiments the antigens used were prepared from adult guinea-worms, from embryos of *Wuchereria bancrofti*, and from hydrocele fluids with and without filarial embryos. In a series of 78 cases in which these tests were carried out the results were uniformly positive, both in the infected cases and in the controls, with every one of these antigens. We have now obtained *Dirofilaria immitis* antigen from Dr. Le Sueur of Sarawak, Borneo, and the results obtained with this antigen may be briefly noted here.

Fairley's technique of the preparation of antigen was followed and a 1 per cent saline extract of dried powdered dirofilaria antigen was prepared as follows:—The powdered antigen was incubated in sterile saline for two hours at 37°C., the mixture being shaken from time to time. It was then filtered through a Whatman no. 1 filter paper and a Buchner filter, and then sterilized by passing through a sterile Seitz asbestos filter. The filtrate was put up in ampoules and stored in the cold chamber till required for use. Using the extract in quantities of 0.25 e.cm. we found that the antigen produced severe reactions and so the extract was diluted to 0.5 per cent, and 0.1 e.cm. given. The latter dilution was maintained as a standard antigen for all the cases tested. The injection is generally given in the forearm, an injection of physiological saline serving as a control.

Over 250 dermal tests were carried out with this antigen. These were done on cases of filarial infection in its different stages, viz, acute filarial lymphangitis, elephantiasis of the extremities, genitals and breast, filarial abscess, adenitis, varices, cysts and chyluria. There were also four cases of guinea-worm infection. The control cases included, besides healthy normals, cases of kala-azar, epidemic dropsy,

Naga sore, malaria, and other helminthic infections, such as by ascaris, hook-worm and tape-worm.

Most of the filarial cases showed a positive reaction, but, surprisingly, a few cases of ehyluria, heavily infected with microfilariae in the blood, showed no reaction at all. In one patient suffering from filarial cysts four tests were carried out on different occasions; all were negative excepting the second test which showed a very mild positive reaction. As this second test was done shortly after a puncture of a cyst that contained adult filariae was made for examination, it is possible that the release of toxins into the general system by the puncture might have given the slight positive result. The reaction was negative both before and after the cysts were excised.

Signs of obstruction

It is well known that among infected persons living in endemic areas a few develop signs of obstruction even at a comparatively early stage of the infection. On the other hand there are several who harbour the parasite but do not show any manifestations of obstruction for a long time. A few cases of the above types that have been under our observation are mentioned below :

(1) K. B., Hindu, male, aged 28 years: No evidence of filarial infection when examined in 1927. During 1929 a casual examination of the blood revealed microfilariae in it. He suffered from orchitis once every 2 to 3 months during 1929-30.

(2) A. G., Sepoy, Mohammedan male, aged 21 years, native of North-West Frontier Province (non-endemic area); stationed at Dinapur, Behar (endemic area): Developed lymphatic obstruction of the inguinal region due to filarial infection after 18 months' stay.

(3) M. O., European, male, aged 24 years: First visit to India 2 years ago; residing in Kidderpore, Calcutta (endemic area), for last 2 years. First sign of filarial infection (lymphangitis left leg) noticed six months ago.

(4) M. N. M., Hindu, male, aged 40 years: Occasional examination of peripheral blood during the last ten years showed the presence of microfilariae. No signs or symptoms of filarial disease present.

(5) S. M. J., Hindu, male, aged 48 years: Microfilariae in blood were present on every occasion we examined it during the last seven years. No sign or symptom of filarial disease up to date.

(6) S. R., Hindu, male, aged 28 years: Blood examination for microfilariae was carried out twice during 1930, seven times at varying intervals during 1931-32 and in February 1933; microfilariae were found on every examination of the blood. Patient shows no signs or symptoms of lymphatic obstruction.

Individual susceptibility, therefore, is an important factor in the manifestation of signs and symptoms of filarial infection.

From the foregoing considerations it will be seen that filarial patients can be broadly classified into three types, (a) non-susceptible, (b) moderately susceptible, and (c) highly susceptible. The non-susceptible class show microfilariae on examination of blood and high eosinophilia, but do not show any obvious signs of the disease. These persons harbour the parasites

for several years without any apparent injury, as can be seen from the cases already reported, and are the main source for the spread of the infection. Dermal test shows uniformly positive but mild reactions in all of them.

In the second type (moderately susceptible) we find that there is lymphatic block with the result that no microfilariae are found in the blood. In Calcutta, many patients between the ages 18 and 22, including a number of Anglo-Indians, show these symptoms. The most common lesions seen in such patients are the static oedema and lymphatic varix of a mild degree in the arm, leg, or inguinal region. These lesions seem to remain stationary after a certain stage. The patients rarely give a history of having suffered from acute lymphangitis. They improve rapidly under treatment, remaining free from further infection. Eosinophilia is moderate and dermal tests give slightly more severe reactions.

The highly susceptible are those who develop obstruction quite early and remain susceptible for further infections. They suffer from periodical attacks of lymphangitis, each attack aggravating the lymphatic blockage and bringing about changes in the glands, lymphatic vessels and skin. Microfilariae are usually absent from the peripheral blood in these cases and eosinophils are practically normal. In these, dermal tests show acute reactions. Secondary infection plays an important rôle and severe pathological changes are quickly brought about. Advanced cases of elephantiasis of the limbs, genitals, and breast belong to this class.

Intensity of filarial infection

We shall now briefly discuss the various factors which influence the infection in a given area. Of these the more important are, (a) optimum atmospheric conditions, (b) the density of human population, and (c) the density of mosquito population.

By the term optimum atmospheric conditions we mean the most favourable temperature and humidity conditions for the transmission of filarial infection. It has been found that a temperature ranging between 80° to 90°F. and a relative humidity of above 60 are necessary for the normal development of the filarial embryos in the mosquito. It has also been observed that any deviation of the temperature and humidity affect adversely both the mosquito and the parasite undergoing metamorphosis in the mosquito. From a record of the daily average temperature and humidity observations in any given area we can mark out the period with the optimum temperature and humidity conditions necessary for the transmission of the infection. This period, which may be termed 'the effective period of infection', varies from place to place according to their physiography; it may be from April to October, as in Calcutta, or throughout the whole year, as in Cochin.

When there is crowding in an endemic area the chances of the number of carriers is great and thus the transmission becomes easier. In small villages owing to the thinness of population the disease is practically absent. An instance of village immunity may be mentioned here. The whole population of the village Osmanpur in Behar was examined for filarial infection, and, although in the adjacent town Purulia—which is only five miles from the village—one ward of about the size of Osmanpur showed a microfilaria rate of 7.5 per cent, no infection could be detected in the village. Surveys have been carried out in several villages, such as Khoira, Champati, Tulsipur, Bhaipur, Gangarampur, and Chagal, which are situated near endemic towns, Cuttack and Midnapur, and the results corroborate the above conclusion.

Infection is heaviest in towns and big densely populated villages, but is low in the cities. In the latter the good drainage and the piped water supply afford hardly any chances for mosquito breeding on a large scale, while in smaller towns and big villages conditions are more favourable for their breeding owing to the inefficient drainage and the uncovered water supply, chiefly from wells and tanks. In many of these places there is a pernicious system of building catch-pits for sullage and bath-water, and all these places afford excellent breeding grounds for mosquitoes.

We shall now see how these factors affect the incidence of filarial infection in some typical endemic areas.

high as in hyperendemic areas, but a satisfactory drainage system and good sanitary conditions keep down the number of *Culex* breeding-places in the city to a comparatively low figure. Furthermore the heavy rainfall during the months July to September tend to wash out the breeding-places and the mosquito population is exceptionally low. With the onset of the cold weather the mosquitoes increase in number but the most favourable period for transmission has now passed. It is seen therefore that the synchronization between the periods of transmission and mosquito breeding is reduced to the three months, April to June, and hence the comparatively low microfilaria rate of the city (9.1 per cent).

The incidence of filarial disease in Calcutta is 5.3 per cent, in spite of the microfilaria rate being only 9.1 per cent. These figures show a proportionately higher rate because of the fact that a large number of persons with filarial diseases come to Calcutta for treatment and are included in our statistics. For the same reasons, it is not possible to discuss the type of filarial lesions in relation to the microfilaria rate as one finds all types common.

Cochin.—This town is situated on the sea on the northern end of a long narrow peninsula, separated from the mainland by a backwater. It is very densely populated and has a climate which is hot and moist all the year round. Rainfall is heavy, chiefly received during the south-west monsoon. The following table shows the average monthly temperature, rainfall, and humidity observations at Cochin :

Monthly and annual normals, Cochin

Month	TEMPERATURE		Humidity at 8 hours	Rainfall	Number of rainy days
	Maximum	Minimum			
January	89.3	71.8	73.0	0.78	1.0
February	90.2	74.0	75.0	0.90	1.5
March	91.4	77.2	77.0	1.96	2.7
April	91.6	78.4	77.0	5.00	6.3
May	89.7	77.5	81.0	11.65	12.7
June	85.3	74.8	87.0	29.11	24.4
July	83.8	74.0	88.0	23.35	23.6
August	84.1	74.4	86.0	12.25	18.5
September	84.9	74.5	85.0	9.28	14.2
October	86.6	74.7	84.0	13.22	14.3
November	87.7	74.4	80.0	6.24	8.2
December	88.7	72.8	74.0	1.69	2.5
NUMBER OF YEARS ON WHICH THE DATA IS BASED.	33	33	22	51	51

Calcutta.—The effective period of infection for Calcutta is about seven months, April to October. Considering the crowding in the city and a fairly long period of transmission, the microfilaria rate might be expected to be as

It is seen that there is very little variation in the mean temperature and the high humidity during the whole year. Cochin therefore affords the very best climatic conditions for transmission of filarial infection.

There are open drains and ponds, in which coir is steeped, scattered all over the place, so that with the moderate temperature and humidity the conditions are particularly favourable for the breeding of *Culex fatigans*, practically all the year round. The effective period of infection for Cochin appears to be practically throughout the year and the microfilaria rate is above 20 per cent. Here the age incidence for filarial diseases is 8 to 10 years on account of the heavy infection. The filariae very rarely reach maturity in the main abdominal lymphatics, so that hydrocele, chylocele and chyluria are not usually observed as the obstruction of the distal lymphatics (i.e., the inguinal or epitrochlear) occurs very early in life. The superficial lymphatics are first involved and here the elephantoid conditions of the legs, arms, breast, etc., are seen as the most common clinical manifestation of filariasis.

As regards the relation between the period of infection and the microfilaria rate for Cuttack, Puri and Allahabad reference may be made to our previous paper (Aeton and Rao, 1930).

Relation between the intensity of infection and types of filarial diseases

In this same paper (Aeton and Rao, 1930) it was shown that there is intimate connection between the intensity of infections and the types of lesions produced. In hyperendemic areas the blockage is at the most distal set of glands and therefore the lesions are chiefly elephantiasis of the limbs. In areas of moderate endemicity the blockage occurs higher up and thus all types of filarial diseases are common. In areas of low endemicity the parasite is able to reach the juxta-aortic region and cause partial obstruction giving rise to varix and chyluria. No elephantiasis is seen in these areas.

(b) DUE TO SECONDARY INFECTION

We may now consider the pathological conditions produced by the secondary organisms. In a large percentage of infected individuals as the filarial parasites prepare the nidus the secondary infection plays an important rôle in the causation of lymphangitis, complete lymphatic obstruction, and rapid pathological changes in the tissues and skin. The most common organisms met with in these lesions are the streptococci and *Staphylococcus albus* and *aureus*.

Streptococci bring about acute attacks of lymphangitis, cellulitis or periadenitis producing elephantiasis, as in elephantiasis nostra. The organisms are usually derived from some focus, either external or internal, and can sometimes be isolated from the source as well as from the acute lesion. The mechanism by which they appear in the local areas has already been described in a previous paper (1929). Buxton (1928) suggests that the acute attacks of lymphangitis may be classified as centrifugal

or centripetal, according to the direction in which the inflammation spreads. This may be a guide to the source of the secondary infection. The various clinical diseases produced by these cocci in filarial patients are filarial colic, endemic funiculitis, abscess, cellulitis and general septicæmia. All these are of an acute and virulent nature. Death in filarial colic is usually the result of acute septicæmia and toxæmia, and in endemic funiculitis it is due to generalized peritonitis. In all these infections the fever is high, 103°—105°F., with a rapid pulse and a marked leucocytosis.

The chief clinical manifestations due to staphylococci are periadenitis, lymphangitis and abscess. The tissue reaction produced by these organisms may be distinguished from purely filarial infection by the nature of the exudate and the results of the culture. In the filarial infection they may undergo caseation and softening, and the pus is sterile. The fever is very slight and the leucocytosis is moderate.

Microscopical anatomy

We will now describe the various pathological changes that take place in the lymphatic glands, vessels and the skin in filarial infections, due to the parasite itself and to the secondary infection.

(a) *Changes in the lymphatic glands and vessels*

The filarial larva escaping from the proboscis of the mosquito enters the human skin, travels along the afferent lymphatics and enters the lymphatic gland. It reaches the medulla of the gland through the space between the trabeculae and the lymphoid nodules of the cortex. The dense reticular tissue of the medulla renders the passage of the larva through it difficult. Sometimes the larva is held up and destroyed by the endothelial cell granulation tissue. Giant cells are formed near the dead worms. The granulation tissue becomes vascularized by the formation of new blood vessels and is gradually converted into fibrous tissue, the process resulting in a scar in the medulla of the gland.

When a large number of filarial larvæ pass through a gland, the whole gland increases in size and in a short time is converted into a mass of eosinophil granulation tissue. As the lymph channels are obstructed by the granulation tissue, lymph can no longer percolate through the gland and the filarial larvæ also cannot pass through it. The afferent vessels are blocked, the lymphatic pressure rises and the vessels below dilate, particularly those of the hilum of the distal lymphatic gland. A complete description is given in the paper on 'Kataphylaxia' (Aeton and Rao, 1929).

Stages of elephantiasis

In describing the pathological changes in elephantiasis, it will be convenient to divide them into three stages, the first stage being

static œdema due to the effect of filarial toxin on the tissue permeability, the second lymph stasis with the formation of blubbery mass, and the final pachydermia stage due to the secondary infection of the skin added to the above.

Static œdema

When there is lymphatic blockage the toxins are confined mostly to the affected limb and are dammed back by the obstruction. The toxin possibly brings about an increase in the permeability of the tissue cells in the affected limb and causes static œdema which is aggravated by posture as in standing. In Calcutta, one finds this type most commonly in individuals between the ages of 18 to 22 years. Our records of the filariasis clinic show a surprisingly large number of Anglo-Indian girls, mostly typists, telephone operators and nurses under this head returned as 'lymphangitis—afebrile'. Ankles, feet and legs are chiefly affected; the affection is usually one-sided. The swelling reaches its maximum towards evening, clearing almost completely by rest overnight; the œdema pits on pressure, and the skin is otherwise normal; the attacks of swelling tend to recur periodically; the inguinal or axillary glands are very slightly enlarged and tender, and the main lymphatic vessel is thickened. These patients complain that periodically a small lump, the size of a pea, appears along the course of the main lymphatic, travels downwards gradually, and then disappears. This small lump is an aberrant migrating parasite which irritates the tissues, causes induration and sometimes forms a permanent cyst-like swelling in the legs or arms. The dermal tests are positive in every one of these patients tested. The microfilaria rate in this stage is fairly high and eosinophils range from 300 to 500 per c.mm. All these cases come from the hyperendemic areas of the city.

Second stage—Blubbery tissue

The œdema increases till it becomes more or less permanent. The subcutaneous tissue absorbs lymph and forms what is known as the 'blubbery mass'. When such a mass is cut out it is found to consist chiefly of lymph and white fibres. During this stage the limb has a smooth, glistening appearance, and pits on pressure. Lymphangitis recurs periodically in the affected limb and every attack aggravates the œdema and fibrosis. There is usually a tendency to the formation of abscesses, either along the main lymphatic vessel or in the devitalized tissue of the limb. As in the case of lymphangitis during this stage the abscess may be due to helminthic, or to secondary infection. The lymphatic obstruction is now almost complete, so that the filarial worms cannot proceed further along the vessel and aberrant migration takes place. Fugitive swellings and lymph-cysts appear in the limb. The microfilaria rate and eosinophilia are very low. A number of x-ray photographs have been taken of the

extremities and pelvic region in such cases. Figure 4 shows an opaque area in the inguinal region indicating calcified worms in a case of elephantiasis.



Fig. 4.—Skiagram showing opaque area of calcified worms in the left inguinal region in a case of elephantiasis of the left leg.

The pathological changes in the glands may be briefly described. The irritation of the glands, the destruction of the immature parasites by the reticulo-endothelial tissue and the gradual replacement of lymphoid tissue by fibrous tissue result in the hypertrophy of the gland; in hyperendemic areas the epitrochlear and inguinal glands are most commonly involved. On account of the short period of infection such conditions are rarely seen in areas of moderate or low endemicity. As the source of irritation is not continued for a sufficiently long period in these places the glands which are affected show enlargement only for a short period and then shrink down in the absence of irritation. When the hypertrophied gland is cut into it shows a fibrous mass with very little lymphoid tissue. Generally such glands do not contain parasites. The worms mature below the hypertrophied gland and the embryos which cannot reach the blood are destroyed in the tissues, thus aggravating the fibrosis. This leads to the third stage described below.

Third stage—Pachydermia

While in the first two stages the changes in the tissues are chiefly the result of filarial toxin and lymph stasis the third stage is brought about by the addition of secondary infection of the skin (epiblastic kataphylaxia). The defence mechanism of the surface layer or epidermis is gradually being impaired as the elephantiasis of the part is increasing in size. As the lymph

cannot be properly drained away from the surface areas, owing to the blockage of the terminal villous lymphatics in the papillae and owing to inflammatory changes in the junctional vessels in the region of the subpapillary plexus, it accumulates and percolates upwards to the prickle cells layer producing hypertrophy of the papillae. At the same time the keratinization of the horny layer is interfered with, so that the mechanical protection afforded by this layer is partially or completely lost. On the upper aspect of the foot and instep, and in the scrotal skin, groups of these terminal lymphatics may be involved in this obstructive inflammatory lymphangitis, so that the epidermis is thrown into large papillomatous growths and the dilated terminal lymphatics are seen giving rise to the so-called lymphatic cysts of the skin. Deep fissures form in the papillomatous area, owing to movements of the limb and the rigidity of the tissues of the corium, and the tissues are very prone to attack by secondary septic infections from the surface. Secondary streptococcal and staphylococcal infections under such conditions more usually come from foci situated on the skin surface.

Diagnosis of elephantiasis of filarial origin

Considerable difficulty is often experienced in distinguishing diseases such as dermatolysis, from elephantiasis of filarial origin. The former also cause swelling of the extremities and thus resemble true elephantiasis outwardly. The important points of diagnosis of elephantiasis of filarial origin are (1) a knowledge of the distribution of filarial infection and (2) history of the patient which were discussed in a previous publication (Acton and Rao, 1931). In doubtful cases a microscopic examination of the sections of the tissue will reveal the true nature of the lesion, for example in fibromatosis the changes are essentially a hypertrophy of the skin; these can be easily distinguished from the changes in elephantiasis.

Summary and conclusions

(1) The early history of elephantiasis and its differentiation from a group of diseases showing similar signs such as leprosy and Madura foot is traced. It is shown that cases of dermatolysis, hypopituitarism, elephantiasis nostra, etc., are often mistaken even at the present time for elephantiasis of filarial origin. Some of the common fallacies, for instance, looking for microfilariae in cases of elephantiasis and pitting on pressure as a diagnostic feature, are mentioned.

(2) Apparently-healthy persons may harbour filarial infection for a long time without showing any signs or symptoms. A few histories of infected persons who have been under close examination for about ten years are recorded. Filarial infection produces a low-grade pathogenic toxin, as is evidenced by the fact that in early stages of the infection when microfilariae are present in the blood there is eosinophilia.

Allergic symptoms appear according to individual susceptibility.

(3) Static oedema is the first stage of elephantiasis brought about by the filarial toxin affecting the tissue permeability.

(4) Various factors, such as density of mosquito and human population, and climatic conditions, which influence the prevalence of filarial infection and disease are discussed. The sites of blockage and the time of development of elephantiasis depend upon the intensity of the infection in a particular area. A few typical endemic areas which have been surveyed thoroughly are given as illustrating various degrees of filarial endemicity. In Cochin, where the optimum conditions prevail for the breeding of mosquitoes, the infection is heaviest and therefore the type of filarial disease common is elephantiasis of the extremities. In Calcutta, as a result of better sanitation and drainage the period of mosquito breeding is limited and thus the microfilaria rate is low, whereas the filarial-disease rate is high on account of the large number of imported cases.

(5) The pathological conditions produced by the secondary infections are described in detail.

(6) The various stages of pathological changes in the lymphatic system and the skin are mentioned.

(7) After every attack of lymphangitis the swelling increases. Types of adenitis and periadenitis in hyperendemic areas and in areas of low endemicity are given in detail. The eosinophil count is comparatively low. At this stage the lymphatic blockage is nearly complete, and the stagnant lymph soaking the subcutaneous tissue forms the blubber; errant migration takes place with the formation of fugitive swellings, lymph-cysts, etc. Worms die and get calcified; an x-ray photograph showing the calcified area is reproduced.

(8) The growth of the pachydermia stage is shown. The lymphatic obstruction is complete and therefore microfilariae are not present in the peripheral circulation. Worms die and form abscesses along the lymphatic channels. The toxin, and the pressure of stagnant lymph with the changes due to secondary infection, both from within and from outside (epiblastic katablaxia), complete the formation of the final stage of elephantiasis.

(9) Several conditions of lymphatic obstruction which are not due to filariasis are known. Clinical mistakes are often made owing to the difficulty in the differentiation of true filarial elephantiasis from this.

REFERENCES

- Acton, H. W., and Rao, S. S. (1929). The Importance of Secondary Infections in the Causation of Filarial Lymphangitis. *Indian Med. Gaz.*, Vol. LXIV, p. 421.
Acton, H. W., and Rao, S. S. (1929). 'Kataphylaxia', A Phenomenon seen Clinically in Filariasis. *Ibid.*, Vol. LXIV, p. 601.

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TREATMENT OF CHRONIC INTESTINAL AMOEBIASIS WITH CARBARSONE

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THE difficulty of curing chronic amoebiasis is well known to physicians practising in the tropics. An acute attack of amoebic dysentery even in the majority of cases be successfully relieved by proper treatment, but eradication of the chronic intestinal infection with *Entamoeba histolytica* is a difficult matter. A large number of remedies are supposed to cure this condition, but most of these reduce the infection to a low level, so that the patient's own natural powers of resistance can keep in check the parasites which still remain in the body. Many of these patients become carriers.

Of the drugs used against amoebiasis emetine, although it is an excellent drug in acute amoebic colitis, often fails to cure the chronic condition. Halogenated oxyquinoline derivatives, such as yatren (loretin, quinoxyl), ehiniofon, vioform, etc., were highly spoken of but have proved disappointing. Some dye derivatives such as Rivanol (2-ethoxy-6:9 diamino acridine) and bismuth subnitrate have been tried with no better results. Acton and Chopra (1931 and 1932) tried the bismuthous iodide compound of the total alkaloids of *Holarrhena antidysenterica* in doses of 10 grains twice a day by the mouth for 10 to 20 consecutive days and they cured 73 per cent in a series of 78 cases. These results are considerably better than those obtained with any other drug tried by the senior author. The difficulties of obtaining satisfactory bark and of extraction of the alkaloids without producing decomposition, which renders them inert from the therapeutic point of view, are however considerable, and have been pointed out by these workers. The failures of kurehi alkaloids in the hands of Leake (1932) can thus be explained.

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Acton, H. W., and Rao, S. S. (1930). Urticaria due to Filarial Toxin. *Ibid.*, Vol. LXV, p. 130.

Acton, H. W., and Rao, S. S. (1930). Factors which Determine the Differences in the Types of Lesions produced by *Filaria bancrofti* in India. *Ibid.*, Vol. LXV, p. 620.

Acton, H. W., and Rao, S. S. (1931). The Diagnosis of Lymphatic Obstruction of Filarial Origin. *Ibid.*, Vol. LXVI, p. 11.

Buxton, P. A. (1928). *Researches in Polynesia and Melanesia*. London: The London School of Hygiene and Tropical Medicine.

Hamilton Fairley, N. (1931). Serological and Intradermal Tests in Filariasis. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXIV, p. 635.

Taliaferro, W. H., and Hoffman, W. A. (1930). Skin Reactions to *Dirofilaria immitis* in Persons Infected with *Wuchereria bancrofti*. *Journ. Prev. Med.*, Vol. IV, p. 261.

During recent years some organic compounds of arsenic have been tried in chronic amoebiasis. Stovarsol or acetarsone (3-acetyl-amino-4-hydroxy-phenyl-arsinic acid) was the first compound of this series which could be given by the mouth and it was tried in this condition, but the drug showed no curative action whatsoever in intestinal amoebiasis. Treparsol (3-formyl-amino-4-hydroxy-phenyl-arsinic acid) has also been tried, but with no better results. Leake (1932) suggested that carbarson (4-carbamino-phenyl-arsinic acid) had better amoebicidal properties than any of the other arsenicals. Reed and his co-workers (1932) tried it in a small series of cases and found it to be very effective and non-toxic.

Carbarson belongs to the original series of organic arsenicals prepared and tested by Ehrlich and Berthelm as long ago as 1909 and has the chemical formula $H_2O_3AsC_6H_4NHCONH_2$ being 4-carbamino-phenyl-arsinic acid. It is a white crystalline solid without odour or taste; it is stable in air and contains 28.85 per cent of arsenic when anhydrous. It is practically insoluble in water, but dissolves in alkaline aqueous solutions; it melts at 174°C. It is readily absorbed after oral administration and is excreted in the urine at about the same rate as stovarsol. Experimentally it is less toxic than stovarsol and has more powerful amoebicidal properties, its 'therapeutic index' being about eight times as favourable as stovarsol. As it contains a substituted amino-group in the para position to the arsenic atom, its liability to injure the optic tract should be borne in mind. No untoward symptoms were, however, observed after continued administration of the drug to laboratory animals in doses within the therapeutic range. Carbarson has been recently put on the market by Lilly & Co., of Indianapolis, U. S. A., and is sold in pulvules of 0.25 gramme ($3\frac{1}{4}$ grains) each.

After reading about the encouraging results obtained by Reed and his co-workers the senior author tried the drug in a series of patients in the wards of the Carmichael Hospital for Tropical Diseases. The patients were mostly suffering from chronic amoebiasis and the majority of them had had repeated attacks of dysentery. The drug was prescribed in doses of 0.25 gm. twice daily for 10 consecutive days in gelatine capsules by the mouth. The patients were kept on ordinary diet and, except a saline purgative whenever required to relieve constipation, no other drug was given.

The criterion of cure applied in this series was five or more negative examinations of the stools on different days after the cessation of all treatment. As has been pointed out in a previous paper, it is fully realized that it cannot be claimed that all such cases were really cured. However it is the best criterion that can be practically employed and from experience we know that five negative examinations indicate

in most cases a favourable prognosis if not a definite permanent cure. The difficulty of keeping the patient in the hospital when once the acute symptoms are relieved is very great, so for all practical purposes we had to accept this criterion. Whenever possible more examinations were made.

The records of 31 cases in which the drug was tried are given in a table which is self-explanatory. Out of 31 patients 23 (74.2 per cent) were cured, in 4 (12.9 per cent) the drug failed and in 4 (12.9 per cent) the result was indeterminate. As regards the indeterminate cases, although the patients left the hospital before the usual five examinations of the stools could be carried out, considerable improvement was noticed in their general condition after the treatment. A perusal of column 3 will show that the majority of the patients had suffered from the disease for long periods, and that many of them showed cystic forms of *E. histolytica* and had Charcot-Leyden crystals in their stools. The separate cure rates in vegetative and cystic forms of infections are given below and it will be seen that the drug is equally effective in either condition.

	Total	Cures	Indeterminate	Failures
Vegetative	11	8 (72.8%)	2 (18.2%)	1 (9%)
Cystic	20	15 (75%)	2 (10%)	3 (15%)

The proportion of probable cures to failures in this series is 5.75:1, as compared with 3.5:1 obtained by Knowles (1928) with emetine bismuthous iodide in a similar series of chronic cases.

Among the failures it is interesting to note that out of four cases only one had vegetative forms of *E. histolytica* and three had the cystic form. Some of the patients were infected with bacillary dysentery also, in addition to the amoebic infection. These were the most difficult to cure, but a course of autovaccine given either preceding or along with carbarsone treatment often brought about a cure. In case no. 27, carbarsone failed, but extractum kurchi liquidum with liver extract was effective. The usual course of carbarsone failed to cure case no. 7, but a cure was effected by a course of emetine bismuthous iodide 2 grains daily for 10 days.

It may also be noted here that in this series no untoward symptoms of any kind were produced either on the eyesight (due to the *para* position of the substituted amino-group), on the gastro-intestinal tract, or on any other organ or tissue of the body, by administration of the drug in doses of 0.25 gramme ($3\frac{1}{4}$ grains) twice daily for 10 days. Even those patients who were not cured improved in health generally, on account of the tonic and stimulating effects of arsenic on the system. Continuation of the drug for longer periods is now being tried in patients who have failed with the usual course of 10 days.

TABLE

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
1	K. P. ..	H., M., 22	1 year; emetine	<i>E. h. veg.</i> , C.-L. crystals, <i>B. lactis aerogenes</i> .	Carbarsone 0.25 gm., b.d., for 10 days.	Scanty <i>E. h. veg.</i> C.-L. crystals.	Failed.
2	B. R. ..	H., M., 26	2 years	<i>E. h. veg.</i> and cyst. C.-L. crystals.	Do.	Negative 6 exams.	Cured.
3	A. A. ..	M., M., 28	1½ months	Scanty <i>E. h. veg.</i> and cyst, H. W. and trichuris ova, <i>B. pseudo-carolinus</i> .	Do.	Do.	"
4	A. H. ..	M., M., 22	1½ years; emetine	<i>E. h. veg.</i> and cyst, giardia cyst, <i>Trichomonas hominis</i> .	Do.	Do.	"
5	H. C. P. ..	H., M., 44	2½ months	<i>E. h. veg.</i> , H. W. ova, giardia cysts.	Do.	Do.	"
6	R. ..	H., M., 40	7 years	<i>E. h. cyst</i> , H. W. and trichuris ova.	Do.	Negative 5 exams.	"

TABLE—contd.

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
7	H.C.G. ..	A.I., M., 40	8 emetine	<i>E. h.</i> veg. and cyst.	I. Carbarsone 0.25 gm., b.d., for 10 days. II. Do. III. E.B.I. grs. ii, daily for 10 days.	<i>E. h.</i> veg. and cyst, giardia cyst, C.-L. crystals. <i>E. h.</i> veg. and C.-L. crystals. Negative 8 exams.	Failed. Cured with E. B. I.
8	B. S. ..	A.I., M., 5	4½ years	<i>E. h.</i> veg.	Carbarsone 0.075 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
9	S.K.M. ..	H., M., 18	Originally admitted for malaria.	<i>E. h.</i> cyst. C.-L. crystals. <i>E. nana</i> cyst. Sputum: pneumococci, <i>M. catarrhalis</i> and short streptococci.	Carbarsone 0.25 gm., b.d., for 10 days.	Do.	"
10	R. B. M.	H., M., 28	10 months	<i>E. h.</i> cyst, C.-L. crystals, microfilaria, <i>B. meta-alkaligenes</i> .	Do.	Do.	"
11	T.A.K. ..	M., M., 50	12 days	<i>E. h.</i> veg., <i>B. proteus vulgaris</i> , H. W., ascaris and trichuris ova.	Do.	Do.	"
12	N.C.M. ..	H., M., 38	2 weeks	<i>E. h.</i> veg., <i>Trichomonas hominis</i> . H. W. ova. <i>B. lactis aerogenes</i> .	Do.	Negative 1 exam.	Indeterminate.
13	N. B. ..	M., M., 25	Originally a case of reticulo-endotheliosis.	<i>E. h.</i> veg., H. W. and ascaris ova.	Do.	Negative 6 exams.	Cured.
14	L. D. ..	H., F., 30	Present attack 4 months. Another attack two years ago.	<i>E. h.</i> cysts. H. W. ova.	Do.	Do.	"
15	A. A. ..	M., M., Ch., 6	Originally admitted for fever with enlarged spleen down to the umbilicus and liver 1½" below costal margin.	Scanty <i>E. h.</i> veg. urobilin.	Carbarsone 0.08 gm., b.d., for 10 days.	Negative 6 exams.	"
16	A.E.C. ..	A.I., F., 22	Irregular temperature for a month following an attack of enteric (<i>B. paratyphosus</i>).	Very scanty <i>E. h.</i> veg.	Carbarsone 0.25 gm., b.d., for 10 days.	Do.	"
17	A. B. ..	H., M., 24	Originally admitted for fever with enlarged spleen.	Scanty <i>E. h.</i> cysts, giardia and H. W. ova.	Do.	Do.	"

TABLE—contd.

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
18	N.K.T. ..	E., F., 31	4 years.	<i>E. h.</i> veg., <i>B. pseudo-carolinus</i> and <i>B. fluorescens</i> .	I. E. B. I. (vomited twice). II. Carbarsone 0.25 gm., b.d., for 10 days. (<i>B. pseudo-carolinus</i>).	Negative 3 exams.	Indeterminate.
19	H.N.C. ..	H., F., 31	Pain epigastric region and waist 12 years. Pneumonia, 12 years ago.	<i>E. h.</i> cysts. Pneumococci, Gram-negative bacilli in sputum.	I. E. B. I. (vomited twice). II. Carbarsone 0.25 gm., b.d., for 10 days and auto-vaccine.	Negative 4 exams.	"
20	S. C. ..	A. I., F., 9	Originally admitted for impetigo; suffered from dysentery when she was only a small baby.	<i>E. h.</i> veg. and cyst. Trichuris ova, <i>B. asiaticus</i> .	Carbarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
21	S.R.G. ..	H., M., 36	Duration of the present attack, 5 years. Dysentery in 1925 also. Liver tender. Indigestion present. Losing weight.	Scanty <i>E. h.</i> veg. and cyst. Blastocystis.	Carbarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	"
22	B. J. ..	A. I., F., 23	Suffered from dysentery when she was 8 years old. Weak and wasted muscles of the right leg and constipation, 9 years.	<i>E. h.</i> and <i>E. coli</i> (veg. and cyst). Blastocystis.	Do.	Do.	"
23	S. ..	H., M., 7	2 years, liver enlarged.	<i>E. h.</i> veg., ascaris ova.	Do.	Do.	"
24	B.R.S. ..	H., M., 9	Pain right hypochondriac region, progressive loss of weight, dyspepsia, 4 years, liver enlarged.	Scanty <i>E. h.</i> veg. and cyst. Blastocystis.	Do.	Do.	"
25	H. J. ..	A. I., M., 11	Originally admitted for low fever, 1 month. Spleen enlarged.	<i>E. h.</i> veg. and cyst. C.-L. crystals. Blastocystis, ascaris and trichuris ova. B. T. rings, trophozoites and scanty gametocytes.	Do.	Do.	"
26	C.C.S. ..	H., M., 30	4 years; last attack 3 months back. Spleen and liver enlarged.	<i>E. h.</i> veg. and cyst, trichuris ova, enterococci.	Do.	<i>E. h.</i> veg. and cyst.	Failed (but cured with kurchi).

TABLE—concl'd.

No.	Name	Race, sex and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
27	R.	E., F., 55	Dysentery last year. Pain right hypochondriac region 3 or 4 months.	Scanty <i>E. h.</i> cysts	I. Carbarsone 0.25 gm., b.d., for 10 days. II. Extract kurchi liquid 5i, b.d., for 10 days and liver extract, one phial, b.d., simultaneously.	Negative 6 exams.	Cured.
28	W. G.	E., M., 34	6 months. Emetine, stovarsol outside.	<i>E. h.</i> cyst. <i>B. pseudo-carolinus</i> , <i>B. asiaticus</i> .	I. Carbarsone 0.25 gm., b.d., for 10 days. II. Autovaccine (<i>B. pseudo-carolinus</i>) 2 courses.	Negative 8 exams. on practically consecutive days; negative again after a fortnight.	Cured.
29	R.	H., M., 25	Pain right hypochondriac region.	<i>E. h.</i> cysts. <i>H. W.</i> ova. Fine colonies of yeasts. Sputum: pneumococci <i>M. catarrhalis</i> , yeasts, etc.	Carbarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	"
30	J.	E., F., 24	Dysentery in September last, was treated with emetine with clinical improvement. For the last one month getting pain in abdomen. Had dysentery 31 years ago.	Scanty <i>E. h.</i> cysts. <i>B. pseudo-carolinus</i> .	Do.	Negative 3 exams.	Indeterminate.
31	S.	E., F., 27	3 years.	<i>E. h.</i> veg., blastocystis.	Do.	Negative 6 exams.	Cured.

Abbreviations used:—

A. I. = Anglo-Indian. H. W. = Hookworm. C.-L. crystals = Charcot-Leyden crystals.
 E. = European. *E. h.* = *Entamoeba histolytica*. E. B. I. = Emetine bismuthous iodide.
 M. = Mohammedan. Veg. = Vegetative.
 H. M. = Hindu male. Cyst. = Cystic.
 H. F. = Hindu female.

Summary and conclusion

1. Carbarsone (4-carbamino-phenyl-arsinic acid) belongs to the series of organic arsenicals originally produced by Ehrlich in 1909. It is a white crystalline solid containing 28.85 per cent of arsenic.

This compound has amoebicidal properties and is given in doses of 0.25 gm. ($3\frac{3}{4}$ grains) in gelatine capsules twice daily. In a series of 31 cases a ten-day course cured 23 patients (74.2 per cent), 4 (12.9 per cent) remained indeterminate, and 4 (12.9 per cent) remained uncured. The proportion of probable cures to failures in this series was 5.75:1, as compared with 3.5:1 obtained by Knowles in a similar series with emetine bismuth iodide, and 3.16:1 obtained by Aeton and Chopra with kurchi bismuthous iodide.

The drug produced no untoward effects in the doses administered, and is worthy of further trial in the treatment of chronic intestinal amoebiasis.

REFERENCES

- Acton, H. W., and Chopra, R. N. (1929). Kurchi Bismuthous Iodide: Its Value in the Treatment of Chronic Amoebic Infections of the Bowel. *Indian Med. Gaz.*, Vol. LXIV, p. 481.
 Acton, H. W., and Chopra, R. N. (1933). The Treatment of Chronic Intestinal Amoebiasis with the Alkaloids of *Holarrhena antidysenterica* (Kurchi). *Indian Med. Gaz.*, Vol. LXVIII, p. 6.
 Knowles, R., Das Gupta, B. M., Dutt Gupta, A. K., and Gupta, U. (1928). The Treatment of Intestinal Amoebiasis (an Analysis of Results, and a Review of the Literature). *Indian Med. Gaz.*, Vol. LXIII, p. 455.
 Leake, C. D. (1932). Chemotherapy of Amoebiasis. *Journ. Amer. Med. Assoc.*, Vol. XCVIII, p. 195.
 Reed, A. C., Anderson, H. H., David, N. A., and Leake, C. D. (1932). Carbarsone in the Treatment of Amoebiasis. *Ibid.*, Vol. XCVIII, p. 189.

LETHAL PROPERTIES OF AQUEOUS EXTRACT OF YOUNG BAMBOO SHOOTS*

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INTRODUCTION

It has been mentioned by Watt (1889) in his *Dictionary of Economic Products of India* that the different parts of the bamboo plant possess certain medicinal virtues. The tender leaves are commonly used in the form of a decoction to check diarrhoea in cattle. The expressed juice from the leaf bud is said to be an efficient emetic and an emmenagogue. The cold poultice made from the tender shoot is considered by villagers in guinea-worm-infected areas to be an efficacious application for the dislodgment of worms from ulcers. In a previous report on the subject (1932) it has been shown that the aqueous extract of the young bamboo shoot possesses, in addition, definite larvicidal and insecticidal properties. In this paper we have recorded the results of preliminary observations made to find out the active principles responsible for these different properties of bamboo shoots and also to determine the possible utility of these in larval and insect control measures.

EXPERIMENTAL OBSERVATIONS

(1) *Preparation of the extract.*—The outer coverings of the young bamboo shoots, about 1 to 1½ feet in height, were peeled off, till the soft inner core was reached. They were then cut into small pieces which were well pounded and the juice was expressed from them. This, after dilution with an equal quantity of water, was used in the following experiments.

(2) *Mosquitoes and mosquito larvæ.*—*A. stephensi* mosquitoes and their larvæ were used to test the toxic effect of the drug, since the preliminary observations showed that, of the different species of mosquito larvæ tested, these resisted the action of the drug for a relatively long time.

(3) *The species of bamboo used in the experiment.*—

- (i) *Dendrocalamus strictus*,
- (ii) *Bambusa affinis* (Munro), and
- (iii) bamboo shoots that are commonly sold in the market as a vegetable.

From the literature available, neither the chemical composition nor the medicinal properties of any of the species of bamboo mentioned appears to have been determined so far.

The only species of bamboo that has till now been experimented with appears to be *B. arundanacea*.

Toxic effects of an aqueous solution of bamboo shoot :—

1. *Guinea-worm embryos.*—These are killed by the extract in an average time of 12.5 minutes. The characteristic coiling and uncoiling movements of the embryos became gradually diminished and ultimately they were seen to die in a fully stretched condition and not in the fully coiled-up condition, as is usual when they are treated with chemicals, such as formalin or perchloride of mercury.

2. *Cyclops.*—The extract kills the cyclops in an average time of 10 minutes.

3. *Maggots of the house-fly.*—The extract kills the maggots in about 45 minutes.

4. *Adult flies.*—When a cotton-wool plug soaked in the extract was placed beneath a test-tube containing adult flies, they were seen to die in the course of 7 minutes.

5. *Adult mosquitoes.*—When a cotton-wool plug soaked in the extract was placed beneath a test-tube containing adult mosquitoes, they were seen to be killed in an average time of 3.5 minutes.

6. *Eggs of A. stephensi.*—250 c.cm. of water was taken and to this 2 c.cm. of the bamboo shoot extract was added. The eggs that were placed in this solution did not develop into larvæ while those placed in the control tube, containing 250 c.cm. of tap water only, developed into larvæ, pupæ, and finally into adult mosquitoes.

(A) Laboratory observations

(i) Undiluted extract, i.e., the expressed juice from the bamboo shoots without the addition of any water, kills the larvæ in an average time of 15 minutes. Under similar experimental conditions, a 5 per cent solution of potassium cyanide takes 22 minutes, and 1.2 per cent of hydrocyanic acid (B. P.) takes 19 minutes to kill the larvæ. The times taken to kill the larvæ by the bamboo-shoot extract, potassium cyanide solution and hydrocyanic acid solution respectively of different strengths are given in tabular form below.

(ii) One hundred c.cm. of the 50 per cent strength extract was taken in a Petri dish and the time taken to kill the larvæ by this was observed every day for a period of 25 days, at intervals of every 24 hours, the extract being kept exposed to the atmosphere during this period to facilitate the diffusion of hydrocyanic acid formed, into the air. The results of the observations have been expressed in the form of a graph. As is evident from the graph the toxic effect of the extract was at its maximum at the end of 24 hours on the second day of the experiment and then the extract became less and less toxic till the 6th day of the experiment when it took the maximum time of 4 hours and 18 minutes to kill the larvæ. As the

* Paper read before the Indian Science Congress, 1933.

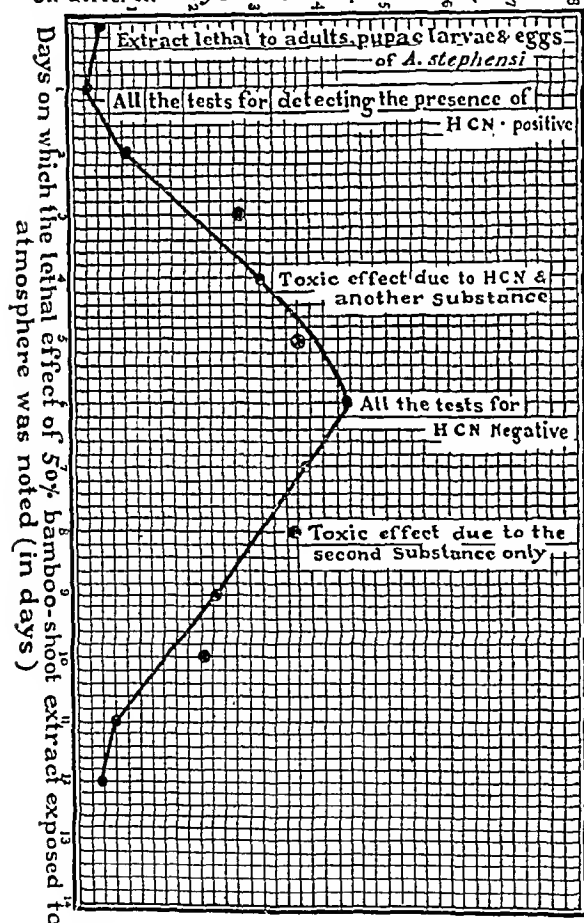
TABLE

Table showing the lethal time for *A. stephensi* mosquito larvæ when treated with bamboo-shoot extract, 5 per cent KCN solution, and 1.9 per cent HCN solution of different strengths

Percentage concentration	TIME TAKEN IN MINUTES FOR LARVÆ TO DIE. AVERAGE OF 15 READINGS		
	Bamboo-shoot extract	5 per cent KCN	1.9 per cent HCN (B. P.)
100	15	21.9	19.5
66.6	15.5	22.2	21.5
50	17.2	25.1	23.2
33.3	26.2	28.7	30.2
25	33.6	29.5	32.5

GRAPH

Average time taken for 15 *A. stephensi* larvæ to die on different days of the experiment (in hours)



solution became more and more concentrated with the second toxic principle, on account of the evaporation of the fluid, its toxic effect on the mosquito larvæ also gradually became increased and was at its maximum again when the volume of the solution was reduced to nearly 10 c.cm. At this period on account of the deposition of heavy solid matter the fluid was

semi-jelly-like in consistency. It was once again diluted to its original volume of 100 c.cm. and the observations continued for another 15 days. This diluted fluid was still toxic to the mosquito larvæ, but it took nearly 24 hours for the larvæ to be killed. Unlike the extract on the first day of the experiment which had a definite toxic action on the adults, pupæ, larvæ, and eggs of the mosquitoes, this fluid was found to have relatively no effect on the pupæ. But it was noticed that the imagines emerging out of the pupæ usually died on the surface of the fluid. Eggs placed on this extract hatched out into larvæ, but these were immediately killed by the extract. Hence this fluid appears to be toxic only to the larvæ and imagines of the mosquito.

From the first to the fifth day of the experiment the extract gave a positive reaction to the following tests for hydrocyanic acid.

- I. Guignard's picrate paper tests (Ghosh, 1930).
- II. Copper acetate benzidine paper test (Sherrard, 1928).
- III. Prussian blue test (Allen, 1930).
- IV. Thiocyanate test (Allen, 1930).

On the 5th day of the experiment all the above-mentioned tests, except the copper-acetate-benzidine test, were negative and on the 6th day all the tests were negative. The extract remained acid to litmus throughout the course of the experiment.

These observations indicate that the toxic effect of the bamboo shoot is possibly due to :—

- (a) the free hydrocyanic acid liberated probably as the result of hydrolysis of one of its cyanogenetic glucosides effected by a specific enzyme,
- (b) another toxic principle either naturally present in the bamboo shoot or formed when the extract is kept exposed to the atmosphere for some days.

The latter conclusion is based on the fact that the toxic effect of the extract on the mosquito larvæ continued when the presence of hydrocyanic acid could not be detected in the extract by the most sensitive tests. This is further supported by the fact that, while it took 22 minutes and 19 minutes for the larvæ to be killed by 5 per cent potassium cyanide solution and 1.9 per cent of hydrocyanic acid solution respectively, it took only 15 minutes for the concentrated bamboo-shoot extract to kill the same species of mosquito larvæ under identically the same experimental conditions, though the percentage of available hydrocyanic acid in the species of bamboo shoots experimented with was not more than 0.6 per cent as determined by Liebig's (Allen, 1930) silver-nitrate method and calculated on the original sample. As is indicated in the graph, the toxic effect of the extract from the first to sixth day of the experiment therefore appears to be due to both hydrocyanic acid and another toxic

substance present in the extract and on subsequent days of the experiment it is due mainly to the second toxic principle, all the available hydrocyanic acid at this period having been hydrolysed and diffused into the atmosphere. As the extract became concentrated with this second toxic principle on account of slow evaporation of the fluid, its toxic effect on the mosquito larvæ also attained its maximum once again on the 12th day. When the solution was once again diluted to 100 c.cm. it still remained toxic to the mosquito larvæ but the time required to kill the larvæ in this dilution was about 24 hours, as contrasted with 15 minutes taken by the original extract on the second day of the experiment, when it contained, in addition, the maximum of hydrocyanic acid liberated.

(B) Field observations

The observations so far made are practically confined to the laboratory findings and till now only a few preliminary observations have been made in the field. When 15 ounces of the concentrated bamboo-shoot extract was added to a borrow-pit measuring about two feet in diameter and three feet in depth and containing a large number of mosquito larvæ, it was found that all the larvæ were killed in the course of about four hours. In addition it was of interest to see, on the next morning, six adult female mosquitoes and two gnats lying dead on the surface of the water. Possibly when these mosquitoes had gone near their breeding place to lay eggs as usual, they were killed by the hydrocyanic acid gas slowly liberated by the action of the specific enzyme on the cyanogenetic glucoside present in the bamboo shoot.

These cyanogenetic plants appear therefore to be a valuable source of hydrocyanic acid and the fundamental difference between the hydrocyanic acid produced by chemical means, as for example by treating an alkaline cyanide with a mineral acid, and that produced by the plant by the action of the specific enzyme on the cyanogenetic glucoside is that by the latter method, which we may call 'nature's method', the hydrocyanic acid is liberated slowly for a long time, about 6 days; and the amount liberated appears to be sufficient to exert a lethal action on the larvæ and adults of insects like mosquitoes, while in the former case, *e.g.*, in the case of 'cyanogas' and liquid hydrocyanic acid (B. P.) which was used as controls, the liberation of hydrocyanic acid and its lethal effect on the mosquito larvæ was noticed only for 4 or 5 hours, under similar experimental conditions.

CYANOGENESIS IN PLANTS

There is as yet no consensus of opinion on the physiological significance of cyanogenesis in plants. In the literature on the subject the following three main ideas as to the significance

of the production of hydrocyanic acid in plants have been traced :—

1. Hydrocyanic acid is an intermediate product in the synthesis of proteins.
2. Hydrocyanic acid is formed by the plant as a means of protection against insect pests.
3. Hydrocyanic acid formed is a waste product of no metabolic significance.

It is generally believed that the specific enzymes are situated in cells different from those in which the cyanogenetic glucosides are present. Whenever the plant cells are destroyed, as by insect pests or when they are crushed as by grinding them, the enzymes are brought in contact with the glucoside and, as the result of the hydrolysis of the glucosides thus effected by the enzymes, hydrocyanic acid is liberated and kills insect pests. In this connection it is of interest to note the opinion held by the famous plant biologist, Dr. Burek (Greshoff, 1906), that the trace of the hydrocyanic acid in the arum plant plays a very special part in the biological process as it gradually narcotizes and kills any insects which may have penetrated into the flower after they have performed their task of self-fertilization. Of significance in this connection also is Guignard's (Armstrong and Armstrong, 1931) observation that exposure of living plants to the action of anæsthetics, like chloroform, and also exposure to severe cold, brings about the interaction between the glucoside and the corresponding ferment. These conclusions are based on the experimental observations made by him on laurel leaves and other cyanophoric plants.

Whatever may be the significance of the presence of hydrocyanic acid in plants, with the few preliminary observations that have been made so far, this method of getting hydrocyanic acid by the hydrolytic action of specific enzymes on the cyanogenetic glucoside appears to be useful and specially suited for insect control measures. With properly-devised methods it may be possible to imitate nature's method of manufacturing hydrocyanic acid and use it for the control of insect pests of mankind, in the same manner as apparently the plant protects itself from its insect pests.

Summary

- (1) Aqueous extract of young bamboo shoots kills cyclops, mosquito adults and larvæ.
- (2) The toxic effect of the extract appears to be due to :—
 - (a) Free hydrocyanic acid liberated as the result of the hydrolysis, possibly of one of its cyanogenetic glucosides by a specific enzyme contained in it.
 - (b) Another toxic substance the nature of which is still under investigation.
- (3) The cyanophoric plants are a valuable source of hydrocyanic acid and with properly devised methods it may be possible to imitate this nature's method of manufacturing

hydrocyanic acid and to apply it in the field for insect control measures; the liberation of hydrocyanic acid by this method being slow as contrasted with chemical methods, the toxic effect therefore lasts for a longer period.

Our thanks are due to Mr. C. C. Calder and Mr. K. Biswas, of the Royal Botanical Gardens, Calcutta, for having kindly supplied us with the bamboo shoots, and also to Dr. Sudhamoy Ghosh, of the Calcutta School of Tropical Medicine, for the kind help given in the course of this work.

REFERENCES

- Allen (1930). *Commercial Organic Analysis*, Vol. VIII, pp. 495 and 504. London: J. & A. Churchill.
- Armstrong, E. F., and Armstrong, K. F. (1931). *The Glucosides*. London: Longmans, Green & Co.
- Ghosh, S. (Translated by) (1930). *Chemical Investigation of Plants* by L. Rosenthaler. London: G. Bell and Sons, Ltd.
- Greshoff, M. (1906). The Distribution of Prussic Acid in the Vegetable Kingdom. *Report, Brit. Assoc.*, p. 141.
- Moorthy, V. N. (1932). Treatment and Prophylaxis of Dracontiasis. *Ind. Med. Gaz.*, Vol. LXVII, p. 617.
- Sherrard, G. C. (1928). Practical Application of Two Qualitative Tests for HCN in Ship Fumigation. *Pub. Health Reports, United States*, Vol. XLIII, Part I, p. 1016.
- Walter, O., Krassnosselska, T., Maximow, N., and Maltschewski, W. (1911). The Presence of Prussic Acid in Bamboo. *Bull. Acad., St. Petersburg*, Vol. VI, p. 397.
- Watt, G. (1889). *The Dictionary of Economic Products*, Vol. I, p. 391.

THE NON-TOXICITY OF PLASMOCHIN AND ATEBRIN

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IN 1931 I introduced in my practice the standard treatment for malaria suggested by Lieut.-Colonel Sinton (1930) in this journal. During that year my assistants and I treated 7,857 cases by one or other of the three courses recommended, including the plasmochin course, and gave to 4,049 children with enlarged spleens quino-plasmochin in *gur* twice weekly, as a gametocidal measure. All malaria cases were treated as in-patients. In 1932, owing to the length of time in hospital involved in the two-weeks and three-weeks treatments, we changed the treatment to the ten-day one suggested by Lieut.-Colonel Knowles (1931) also in this journal. During that year we treated 4,697 cases by this method, and gave to 1,038 children plasmochin simplex for its gametocidal effect, choosing all the children in one line on each garden instead of children with enlarged spleens in all lines.

During these two years no toxic signs appeared in the children treated 'in the field', and in less than half a dozen cases in hospital had we to lessen the dosage of plasmochin, or suspend

treatment till causes of intestinal irritation had been attended to.

It was not until atebtrin had proved its worth very conclusively in other places, that I was able to obtain it for extensive use; but previously I used it in two cases of blackwater fever.

The first was a Punjabi mistri's wife who was seven months pregnant. Partly owing to the pregnancy, she had not followed instructions, and had treated her occasional fever in the way commonly done in the Punjab and Rajputana. Then one morning she woke up about 3 A.M. and found that her urine was black. When seen she complained of fever, vomiting, intense thirst, and pain in the abdomen and back. Her temperature was 101.8°F., and there were dyspnoea, tympanites, tenderness over the liver and spleen, and jaundice. At intervals she was semi-conscious and passed urine involuntarily. What urine could be collected contained blood cell debris. She was treated for one day in the classical way, suggested in *Manson's Tropical Diseases*, ninth edition. Next day she was put on atebtrin, and that night she miscarried, but the placenta was retained. The assistant medical officer removed the placenta manually under far from ideal conditions—the patient was in a house with bamboo mud-plastered walls—taking what precautions were possible. Next day the condition had improved considerably, the jaundice being much less intense. On the following day urine was obtained free from lochia, and was clear and practically free of albumin. Septicæmia followed and was treated concurrently with the atebtrin and plasmochin course. Recovery was uneventful. The patient was advised to seek a district less malarious and left in good health after some months, having had no fever meanwhile.

The second case was in a Bengali clerk's wife, who had had blackwater fever in 1928 and again in 1930. The risk from the third attack, which occurred during November 1932, being considerable, we used atebtrin followed by plasmochin. Her recovery was uneventful, and she has been free from fever since.

I may add that we did not adopt atebtrin in the treatment of blackwater fever because we had had disappointing results with other methods; on the contrary, we have always had excellent results with the 'classical' method, referred to above.

I have now treated five Europeans, and with my assistants, many Indians with atebtrin and plasmochin, and the only trouble we have experienced has been in one European, who on the eighth day of treatment—namely three days after the course of atebtrin was finished—complained of pain in the epigastrium. It was not severe enough to prevent him expressing a wish to attend a parade of the Assam Valley Light Horse that afternoon.

Conclusion

Both plasmochin and atebtrin can be used with absolute safety 'in the field', provided reasonable care is exercised in their administration.

REFERENCES

- Knowles, R., and Das Gupta, B. M. (1931). Clinical Studies in Malaria by Cultural and Enumerative Methods. *Indian Med. Gaz.*, Vol. LXVI, p. 1.
- Sinton, J. A. (1930). A Suggested Standard Treatment of Malaria based upon the Results of the Controlled Investigation of over 3,700 Cases. *Indian Med. Gaz.*, Vol. LXV, p. 603.

RICE INFECTION AND EPIDEMIC DROPSY*

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At Raipur, a village situated in the north-western extremity of the district of Noakhali on the banks of the river Dacathia, Dr. U. C. Nath has built, equipped and staffed a large surgical hospital for the accommodation of his patients. Dr. Nath was in the habit of buying in small quantities the rice necessary for consumption in his family. He varied this practice in February 1930, when a boat containing a large supply of *Balam*† rice, came from Barisal district for sale in his village, Raipur, and from this boat Dr. Nath bought 25 maunds of rice, while a friend, Babu C. R. C., bought 25 maunds and a rice merchant in the local bazar bought the remainder, which was about 25 maunds, for sale in the locality.

There were no cases of epidemic dropsy amongst any people in the village of Raipur, several of whom undoubtedly used the rice from this boat; there were no cases of epidemic dropsy in the house of Babu C. R. C., the members of whose family gradually consumed the rice stocked in his house; but there was a severe outbreak of epidemic dropsy in the house of Dr. Nath, with one death, about eight months from the date of buying the stock of rice. The family of Dr. Nath was the only family that suffered from the epidemic in the populous village of Raipur.

Although all three bought from the same boat, different methods of storing the rice were employed; Dr. Nath stored the rice in a *dol* which is a very big bamboo basket capable of holding several maunds of rice. This kind of basket is prepared by villagers for storing food grains like rice. He smeared the outside of this basket with cow-dung. On the top of the rice stored in this *dol* was put about a seer of lime to protect the stored rice from insects. The *dol* was put upon a wooden platform to protect it from damp and moisture.

After filling the *dol* with the quantity of rice bought from the boat, it was found that there was a balance which could not be accommodated in the *dol*. This remaining rice was stored in a number of gunny bags and in a *matki*, or big earthen vessel, which was kept in the kitchen, to obtain the supply of rice necessary for preparing the daily meal. This *matki* was kept on the floor of the kitchen which was damp. As the stock of rice within the *matki* was exhausted, it was refilled from the stock in the *dol*.

When Dr. Nath bought the 25 maunds of Barisal rice he already had a stock of country rice bought from the bazar; this had to be consumed before he began to use the new rice. It took some time to consume the old stock of rice which was in the *matki* and gunny bags, so that the rice in the *dol* remained undisturbed for about two or three months. However, the exact time of this cannot be definitely ascertained. When using the rice from the *dol*, the upper layer which was mixed with lime was thrown away.

Babu C. R. C. stocked his 25 maunds of rice as follows:—He had in his house several big earthen vessels which were 30 years old. These were soaked in mustard oil some years ago and preserved their oil-soaked appearance at the time when the rice was stored in them. These vessels were kept on bricks. The balance was stored in few gunny bags and this rice was first used up. During the rainy season, i.e., one day in the month of July, Babu C. R. C. exposed his stock of rice for about two hours in the sun, taking it out of the earthen vessels and spreading it out in a thin layer.

The local merchant who bought rice from the boat stored it in a *gola*, which is a small closed circular room made with bamboos and placed on a bamboo platform, but this rice was rapidly used up and did not have long storage, as in the other two cases.

Now in the house of Dr. Nath, nothing remarkable happened for about 6 or 7 months, though all the members of the family used stored rice. At this time there were guests and relatives, who came to stay in the house and lived for two or three weeks and then went away. They were not affected.

Two Christian nurses attached to the hospital obtained cooked rice from Dr. Nath's kitchen, while they prepared other articles of their diet themselves. At the beginning of October 1930, they noticed that the cooked rice that came from Dr. Nath's kitchen was somewhat distasteful and therefore began to purchase their own independent supply of country rice for cooking. These two nurses were found to be suffering from slight cedema of feet, when examined, so they undoubtedly had a mild attack of epidemic dropsy.

About the middle of October, Dr. Nath, while performing a prolonged serious operation in the hospital, found himself so exhausted that he had to sit down for a while and rest during his operation. He afterwards noticed the swollen condition of his feet, but he did not suspect epidemic dropsy. A few days later, Dr. Nath's mother-in-law with two adult female relatives, and three children, one of whom was only a year old, came to the house. At this time the last portion of the stocked rice which was at the bottom of the *dol* was being consumed by the members of the family. Within about 10 days all the members of Dr. Nath's family manifested marked symptoms of

* Rearranged by the Editor.

† *Balam* rice is a parboiled highly-polished rice; it retains little or no pericarp.

epidemic dropsy. The new-comers, who had not been in the house more than 10 days, except the baby who was being breast fed, all became markedly affected like the rest of the family. About this time a guest came to the house and stayed about three weeks. He did not eat cooked rice, but took instead *luchis*, which is a food made from flour, along with other articles prepared in Dr. Nath's kitchen. He altogether escaped being affected with this disease.

Two servants of the house who occasionally took food from Dr. Nath's kitchen and often took food in their own houses were found to be suffering from slight oedema of their feet. Thus, besides the two Christian nurses and the two servants, five adult females, two daughters and one son, aged between 14 and 12, one child aged 3½ years, and Dr. Nath himself suffered from epidemic dropsy and as a result one of Dr. Nath's daughters died with the symptoms of difficulty of breathing and heart failure.

A quantity of rice was sent for examination and the following report was received:

'About 80 per cent of the rice grains were found to be spotted or wholly opaque and damaged, and floating on water-test. On microscopical examination with the low power, several of the rice grains were found to contain yellowish oval bodies, probably eggs of some insects infecting the rice. Bacteriological examination were made after careful external sterilization of rice. Cultures from them showed very numerous varieties of fungi and spore-forming micro-organisms. In some of the plates, there were very numerous micro-organisms with spores at the two extremities with a clear space in the middle. These micro-organisms were Gram negative'.

The study of an isolated occurrence of epidemic dropsy like the present one, though it

leads to no definite conclusion, suggests several points regarding the aetiology and pathology of epidemic dropsy for our consideration.

According to certain writers, the causal organism of epidemic dropsy possesses the characteristic of being changed from a saprophyte to a pathogenic organism by the change of its environmental conditions. The outbreak described in this paper tends to support the above view. For it will be seen that the consumption of the last portion of the rice stocked in the *dol* caused the outbreak not only amongst the members of the family, but also amongst the new-comers, who took the rice only for a short period.

Now if we accept the supposition that a pathogenic micro-organism has appeared in the last portion of the rice, which has caused the disease, it is difficult to explain how this particular micro-organism appeared only in this particular specimen of rice, but this difficulty can be overcome by the supposition that a saprophytic micro-organism in the rice has been changed into pathogenic micro-organism by environmental conditions such as dampness, want of light and air.

The most important practical lesson gained by the study of the epidemic appears to be, that the sunning of the rice, especially during the rainy season, is a good prophylactic against epidemic dropsy.

While epidemic dropsy was caused by preserving rice in a *dol* besmeared with cow-dung outside and kept in a damp room, it was not caused by another sample of the same variety of rice which was preserved in earthen vessels soaked previously in mustard oil. It is possible that mustard oil exerts some preventive action against the appearance of the micro-organism which causes epidemic dropsy. The matter is worth further investigation.

A Mirror of Hospital Practice

A FATAL CASE OF AMBULANT TYPHOID FEVER

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THE following case is of considerable interest on account of the rarity with which such cases are encountered:

A thin, wiry man, aged about 27 years, an employee in the local railway workshop, reported sick on the 13th January, 1933, with a temperature of 103°F., and a history that the attack was preceded by rigors. Malaria was suspected and cinchona febrifuge grs. 10, three times a day, was prescribed and continued for three days.

On the 4th day, the fever subsided to 99°F. in the morning and rose to 102.4°F. in the evening. The patient began passing ten to twenty loose greenish motions a day. He did not feel ill even when the temperature was 102.4°F. His only complaint was of the diarrhoea. The tongue was very clean and continued

to be so till the end. The pulse was in keeping with the temperature and showed no dicrotism. The patient got up to pass his stools. However, enteric fever was suspected, dietetic restrictions were enforced and the patient was warned about the danger of getting out of bed. Bismuth was given for two days, but there was no improvement in the diarrhoea. An acid chlorodyne mixture was prescribed for two more days with the same result.

On 21st January, 1933, the patient was very much exhausted by the diarrhoea. The fever was of a low hectic type, 99°F. in the morning, 100°F. to 102°F. in the evening.

On 23rd January, 1933, he was given bismuth salicylas grs. 90 and tincture opii m. 30 in three ounces of water. The diarrhoea improved very much and the patient felt much better. He was very hungry and consequently neglected the dietetic restrictions and took two tumblers of thick rice *conjee* for the night.

At 12 o'clock that night, he passed a large quantity of blood and slough per rectum. Before 7 A.M. on 24th January, 1933, he had passed half a dozen such motions,

when I was called to see him. The man was very much exhausted, the extremities were cold, there was a gurgling noise in the abdomen, and the right lower quadrant was slightly tender to touch and dull to percussion. He was treated with an ice-bag on the abdomen, ice to suck, morphia hypodermically and calcium lactate in grs. 30 doses by mouth. The hæmorrhage was controlled.

On 25th January, 1933, he passed small dark shiny motions. At 2 p.m. the temperature was 104°F. (reactionary fever?)—the highest recorded during the disease. Morphia gr. $\frac{1}{2}$ hypodermically and calcium lactate by mouth was repeated and a sponge bath was given. The patient could not be confined to bed. He insisted on getting out of bed to go to stool.

On 26th January, 1933, at 8 p.m. he started passing frequent and alarming quantities of blood and slough. In spite of treatment, the man collapsed and died within four hours.

On account of the course of the disease we must assume that the patient continued his work for about ten days after the onset of his illness before reporting sick.

I wish to express my thanks to Dr. J. K. Manson, M.B., Ch.B., my District Medical Officer, for getting me permission to publish these notes.

ACUTE MASSIVE ATELECTATIC COLLAPSE OF THE LUNGS

By S. R. PRALL, M.D. (Cantab.)

MAJOR, I.M.S.

*Acting Civil Surgeon, and Superintendent,
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The following case appears to be worthy of record:—

Mr. N., at. 56, was admitted into hospital on 24th January, 1933, complaining of fever with rigors for the last four days. About three weeks ago the patient had a sharp attack of influenza from which he had not wholly recovered when he got the present attack of fever. He is subject to intermittent attacks of malaria. On admission his temperature was 99.8°F., pulse was 86, and respiration rate 22 per minute. Tongue was clean, lungs clear, and no abnormal physical signs were discoverable. No malarial parasites were seen in the blood. Urine was normal, except for a trace of albumen.

Progress.—Patient complained of some pain in the liver region but on examination there was no tenderness on pressure. The stools were examined on 27th January and nothing abnormal was discovered. It was decided to try the effect of emetine as the fever still continued. For five days following the emetine treatment the temperature remained normal but rose again on the sixth and subsequent days so it was discontinued. Pain and tenderness in the liver region continued and a total leucocyte count showed 25,600 on 6th February. Up to this time, although patient had a slight cough, the sputum was scanty, and no physical signs of bronchitis could be discovered.

On 7th February the routine examination revealed entirely fresh signs. There was dyspnoea with rapid onset, and a sense of oppression rather than pain in the right side of the chest. The distress was marked and the patient seemed acutely ill. The areas of the right upper and middle lobes of the lung were dull on

percussion whereas the base was hyper-resonant—the note being suggestive of a pneumothorax. The liver dulness was pushed down and the diaphragmatic movement on



Fig. 1



Fig. 2.

the right side was definitely impaired. On examination of the heart it was found difficult to map out the area of cardiac dulness but it was definitely made out that

the heart was drawn over to the right side to a marked degree. On auscultation tubular breathing with bronchophony was heard over the areas dull to percussion, while the crepitant râle of pneumonia was conspicuously absent.

The x-ray findings were as follows:—The left lung appeared normal and the left side of the diaphragm moved well. There was a dense shadow in the areas of the upper and middle lobes of the right lung and fixation of the right side of the diaphragm. The base of the right lung appeared normal. The heart was drawn well over to the right side so that the shadow only just extended to the left of the sternum.

The patient was instructed to lie on the unaffected side, and possibly also aided by the movement in carrying him to the x-ray room, improvement in his condition commenced. The physical signs in the chest, on his return from the x-ray room, had changed and moist râles were heard all over the affected areas; the position of the heart was unchanged.

The general condition of the patient continued to improve, the fever ceased and there was no respiratory distress. Sputum, which was now expectorated easily, was muco-purulent and contained no tubercle bacilli.

His improvement was closely followed by use of the x-rays. On 11th February right side of diaphragm moved slightly on respiration and the upper lobe of right lung was clearing. Heart was still over to the right side. On 13th February the range of movement of diaphragm has increased and there is now only a shadow in area of middle lobe. Upper lobe is quite clear. Position of heart unchanged. On 15th February further improvement in diaphragmatic movement. Shadow in middle lobe has diminished. Heart's position not changed. On 21st February lung is now clear and the heart has almost recovered its normal position.



Fig. 3.

Commentary.—The case exhibits the characteristic features of acute massive atelectatic collapse of the lungs. The physical signs, although suggestive of either consolidation or effusion, are distinguishable from both of these

conditions, when it is remembered that the essential part of the diagnosis is the displacement of the heart towards the side of the lesion. The only other condition in which this occurs is fibrosis of the lungs, but when the condition has developed acutely it is always an expression of collapse. A feature of this displacement is the slow return to normal after the lung has become aerated again. In clinical medicine, collapse may be an associate of most of the acute thoracic affections or an accident following many surgical operations, particularly those upon the abdomen. Any tendency to weakness or shallowness of the respiratory activities predisposes to collapse though there is evidence to show that there will always be found actual obstruction of some form or other in the bronchi or bronchioles. The present case is of interest in illustrating the importance of keeping in mind the possible occurrence of collapse in connection with a latent affection of the air passages and lungs.

As regards the direct treatment of the condition, some authorities maintain that exploratory puncture, though no fluid may be obtained, has a dramatic effect in clearing the lung. In the present case, however, turning the patient on the unaffected side was efficacious and resulted in rapid improvement.

I am indebted to Captain N. H. Kulkarni, D.M.R.E. (Cantab.), Radiologist at the Sassoon Hospitals, for the x-ray and radioscopy reports, which were of great assistance.

A CASE OF DIAPHYSIAL ACLASIS

By P. N. RAY, B.A., M.B., F.R.C.S. (Eng.)

(Surgeon, Carmichael Medical College Hospitals, and Additional Surgeon, General Hospital, Howrah)

THIS rare condition is known under a multiplicity of names, e.g., multiple cartilaginous exostoses, hereditary multiple exostoses, etc.

The patient, a Hindu male child aged 12, complained of swelling around both the knees and the left ankle with hard nodules, which were slowly increasing in size. No pain or functional disability was complained of. The condition was first noticed about two years ago.

History of past illness.—No history of rickets. The patient suffered from what was described as a severe sprain of the left ankle, nearly two years ago.

Family history.—A careful enquiry was made with regard to family history. No other brothers or sisters were affected. There was no history of such a disease in the father's line, two generations back. But no such definite information could be obtained with regard to the maternal line.

On examination.—The patient was under-nourished and was below the average height and weight for his age. Multiple exostoses were present in different parts of his skeleton, about the existence of some of which he was unaware. The principal sites were around the knee joints and the upper ends of the humerus and the fibula. Smaller ones were present over the radius, ulna and the ribs. The bones of the face and the skull were not involved. Phalanges were also free from exostoses. Deformity was marked, especially around the knees, but there was very little curvature of the long bones. The proportion between the trunk and the lower extremities was normal. There was hardly any

deformity of the wrists. The patient was quite an intelligent boy.

Radiographic appearance.—Practically the whole skeleton was first examined under the screen and

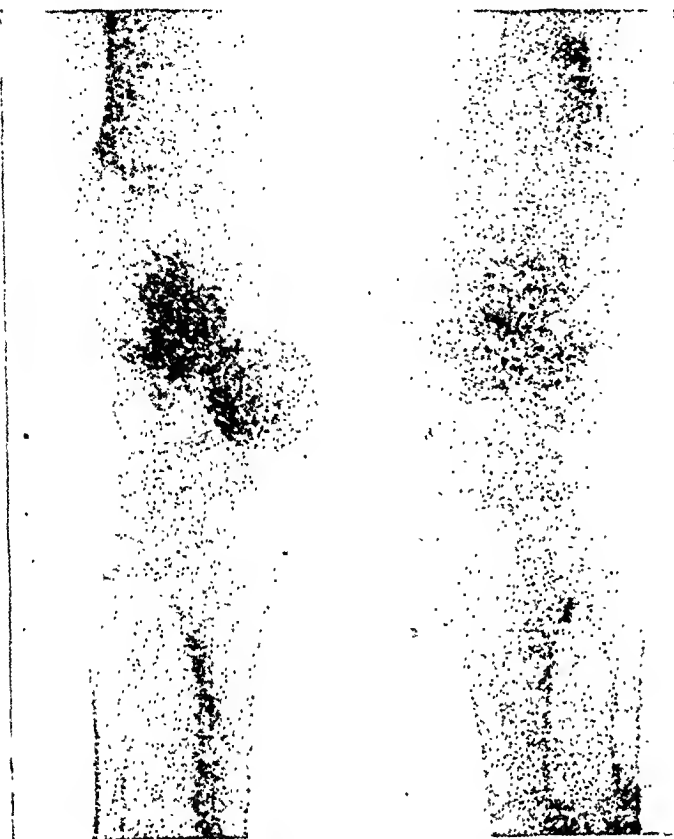


Fig. 1.—Skiagram of both knees, showing the characteristic bony changes.

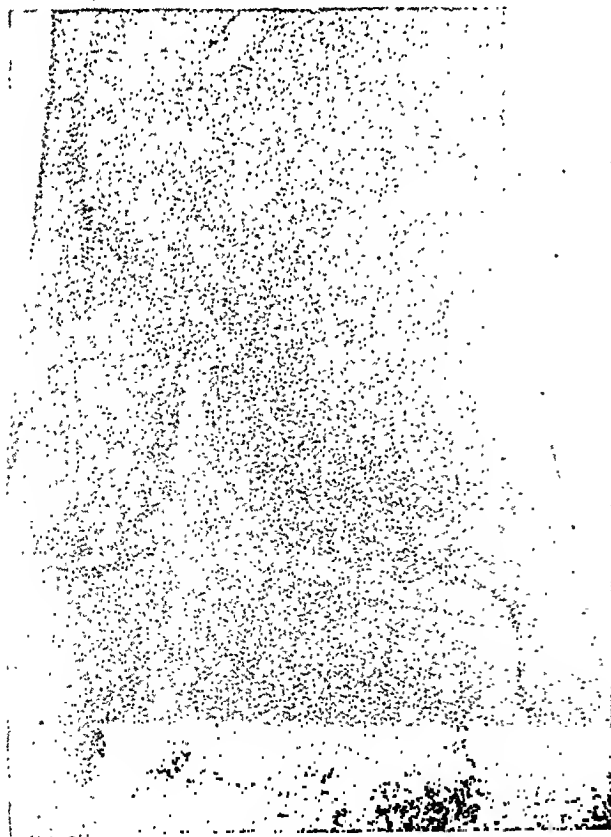


Fig. 2.—Skiagram of the left ankle, showing an exostosis, causing pressure atrophy of the shaft of the fibula.

skiagrams were taken of the parts, where marked changes were noticed.

Proliferative changes.—These are well marked on either side of the epiphyseal line, especially around the knee joint. The lower end of the femur and the upper end of the tibia are converted into cylinders of bone. The epiphyses are also much enlarged and distorted, but no definite outgrowths are present in these regions. But the head of the fibula is characterized by the presence of a distinct epiphyseal outgrowth, which, on the right side, is almost cystic in appearance. Near the diaphyseal ends of the femur and tibia, pointed stalactite-like outgrowths are present (figure 1).

In the diaphysis of most of the long bones, multiple exostoses or osteo-chondromata are present and they show various stages of ossification. Some of these have not passed beyond the stage of chondromata. But apart from the presence of these outgrowths, no great deformity or curvature is noticeable. A fairly large cancellous osteoma is situated near the lower end of the left tibia, causing pressure atrophy of the shaft of the fibula (figure 2).

The patient was advised to report from time to time, and at once on the appearance of pain or functional disability, in the absence of which no operative treatment was advised. This case was first seen by me a year ago and I have seen him several times since.

In conclusion, I have to thank the radiological department of the Carmichael Medical College Hospitals for the excellent skiagraphy.

A PENETRATING WOUND OF THE ABDOMEN*

By P. B. MUKERJEE, L.M.P.

Tajpur, Darbhanga

A HINDU boy aged about 10 was brought to this dispensary from a village four miles off with a tear in the abdomen, through which part of the intestines were protruding.

The history was that on the morning of the same day, he was gored by a bull. The protruding intestines were wrapped in dirty cloths and he was brought at once to the dispensary.

There was a wound about three inches in length and one and a half inches in breadth running obliquely upwards across the left side of the abdomen and terminating at the costal margin; through this a portion of the descending colon and omentum were prolapsed. There was a considerable amount of dirt adhering to the protruding organs. Under chloroform anaesthesia the soiled intestine was cleaned as far as possible with warm normal saline and returned to the abdomen. The wound was stitched in layers, silk being used for the deeper sutures, the skin was closed with horse-hair sutures and a dressing of iodine applied.

Three days later the boy was removed to his home and I saw him nine days afterwards when I found the superficial part of the wound suppurating and gaping widely but the deeper layers appeared to have united satisfactorily. The few stitches that remained in place were removed, the wound was cleaned, packed with iodized gauze and bandaged.

From this time on the wound made satisfactory progress and healed completely in a short time.

* Rearranged by Editor.

Special Articles

THE PRESENT METHODS OF THE KING INSTITUTE IN THE PRODUCTION OF VACCINE LYMPH

By H. H. KING

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(From the King Institute, Guindy, Madras)

Introduction

It is often forgotten that the first generally successful method of preventive immunization was not Pasteur's anti-rabic method but Jenner's vaccination against small-pox. Here in India, where small-pox among the unprotected is all too common, the importance of vaccination is readily recognized. But, while this is so, most medical men are ignorant of the methods used in obtaining a potent lymph; some have even thought that the virus is obtained from small-pox cases. Accordingly, we thought it would be of interest to outline briefly the chief details of our routine methods elaborated in the course of 30 years' experience as an institute. Further, such an account might be useful and suggestive to those working with other viruses. Here, we are not concerned with history; those who are interested should consult *Vaccination and Small-pox in British India* by S. P. James.

Seed lymph

The strain of lymph now used was obtained in 1920 from the Belgaum Vaccine Lymph Depot. This and the strains used by other vaccine institutes in India appear to have been originally obtained from England; importation began in 1802.

Lymph for the inoculation of calves is either ordinary lymph, or lymph obtained from final-passaged cow-calves by a process first of selection and then of passage through other animals. Selection is simply taking lymph for seed only from calves that show the best results. For many years this was the only method used in most vaccine institutes until a striking advance was made by Nijland in Java, who found that the potency (capacity to 'take') was considerably enhanced by using seed lymph that had passed first through a rabbit and then through a buffalo-calf, Nijland's cycle is thus cow-calf—rabbit—buffalo-calf—cow-calf. Until recently this has been the cycle used, but now it has been modified by the addition of a second buffalo-calf to seed cycle. This (King's) modification has still further increased not only the potency but

also the yield of lymph per calf, which has gone up from a previous average of 23 grammes to an average of 30 grammes.

Production of stock lymph

All calves are supplied by contractors who make their purchases in rural areas of the Salem District of the Madras Presidency where apparently bovine tuberculosis does not occur. As a test of this, in 1932, about 200 tuberculin tests were carried out on calves by the double intracutaneous method; all were negative. Supplies of calves are stopped when reports of foot and mouth disease are received from that area. The calves are inspected on arrival at the institute by a veterinary officer and after 14 days' quarantine, they are, if thoroughly healthy, released from quarantine and taken into 'reserve' for use as required. It may be said that illness among these calves is not common. Occasional slight mange or coccidiosis is treated; if severe, the calves are rejected. Usually, the general appearance of the calves improves markedly as a result of good feeding and careful grooming.

On the day prior to operation, the selected calves are shaved on the belly and inner side of the near hind thigh. They are kept overnight in the waiting sheds where special attention is devoted to cleanliness. A clean apron is used to cover the shaved part and this is changed if it happens to become soiled.

When the calves are put on the operation tables, their bellies are washed with soap and warm water, then thoroughly rinsed with warm water, and finally flushed with sterile water and dried with towels. The seed lymph diluted to 1:5 with 50 per cent glycerine is then applied by means of a scalpel. The edge of the scalpel is dipped into the seed lymph and is then used to make an incision about 3 or 4 inches long. The incision is as deep as possible without drawing blood. Perfect incisions are only made after considerable practice. Subsequent incisions prolong the line across the shaved area but stop short half an inch from the hairy margin. At the completion of each line, the back of the scalpel is drawn along the whole line to ensure contact of the lymph with the depths of the incision. Eventually, a series of incisions about $\frac{3}{4}$ inch apart is completed, the appearance of the belly on completion being indicated in figure 1. The total incisions equal about 250 linear inches on the average, but this varies considerably with the size of the calf. The calves remain under the punkah for a quarter of an hour and are then taken to clean sheds where they are prevented from lying down for some hours. After this, clean aprons are used to protect the area of operation. They are inspected after 104 hours and in a small proportion, about 5 per cent, the lesions are judged to be already so mature that the lymph should be removed. The majority are, however, at their best after 120 hours. All lesions are

carefully washed and rinsed and then soaked with a sterile cloth dipped in sterile water to encourage softening. After 5 minutes or more,

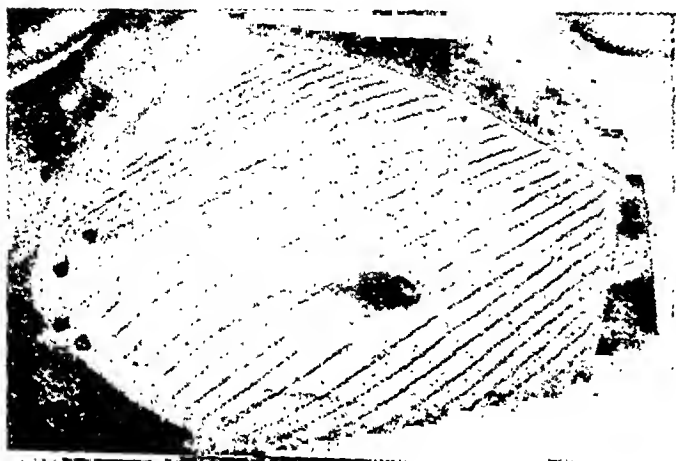


Fig. 1.

when the lesions are dry, the results are carefully scrutinized, and each calf's lesions are classified according to the appearance. A perfect result is given 4 marks, but this is very rare; figure 2 shows an almost perfect result.

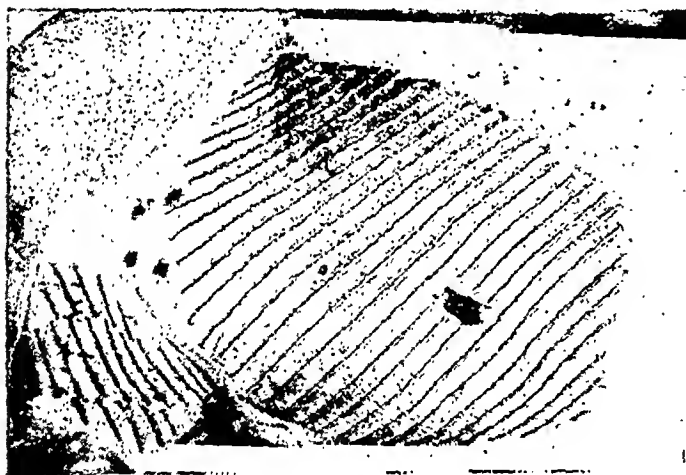


Fig. 2.

The majority earn 2 to 3 marks. Less than $1\frac{1}{2}$ marks leads to rejection while lesions with a value of over 3 marks may be selected for seed. This classification cannot be made without long experience of the work. The lymph is then removed by means of a Volkman's spoon. The operator keeps the line of vesiculation on the stretch with his left thumb and draws the spoon firmly along the whole line, removing all lymph and scab. The contents of the spoon are then scraped off into a bottle which bears a distinguishing number corresponding to the serial number of the calf. This process is repeated until all the lymph is removed when the contents of the bottle are weighed and noted. The yield of six calves, normally those vaccinated with the same strain, is pooled to form a 'cup', i.e., a quantity, roughly 150 grammes suitable for pulping,

storing and testing. Lymph from rejected calves and from specially-marked areas of other calves, where lesions have been damaged, etc., is put in a special coloured bottle, treated with permanganate solution and thrown away.

The removal of the lymph being completed, our original practice was to smear the area with a mixture of vaseline and eucalyptus oil and then to dust with an astringent powder. Recently, this practice has been modified and improved upon by Webster who uses 1 per cent potassium permanganate or Eupad, either of which successfully lessens secondary vesiculation by destroying most of the virus; healing is thus much accelerated. Next day, the calves are handed over to the contractor for disposal. The calves are not killed and so post-mortem examinations are not done. The amount of glycerine (50 per cent) to be added to each 'cup' to give a $1:2\frac{1}{2}$ dilution of the lymph having been calculated, this is gradually added, first in a mortar and later in the course of passage through the pulping machines. Three separate pulping machines of increasing fineness are used and a homogeneous mixture of glycerinated lymph results. This is stored in bottles at a temperature at or just below freezing point—storage at temperatures several degrees below freezing point is quite unnecessary.

Bacteriological tests

Initial test.—A sample of each 'cup' is taken as soon as it is pulped and glycerine solution is added to give a $1:5$ mixture, which is then examined bacteriologically. To estimate the total organisms present, 10 cubic millimetres of the sample is added to 10 cubic centimetres of saline and mixed. Ten cubic millimetres of this is added to melted agar, mixed and poured into a Petri dish. After 48 hours at 37°C . the total number of colonies is counted. About 30 cubic millimetres of the sample is added to (a) litmus milk, (b) broth under paraffin, and (c) cooked meat medium. All these are incubated anaerobically for 48 hours. If any show growth, smears are examined for the presence of spores. The broth culture from three samples (whether showing growth or not) is pooled and 2 cubic centimetres of the mixture is injected intraperitoneally into a guinea-pig. If the animal dies, each broth culture is again tested separately. Subculture from the broth is also made on to agar and, after incubation, a search is made for streptococci. A 'cup' would be rejected if pathogenic spore-bearers, haemolytic streptococci or any pathogenic organisms, other than staphylococci and non-haemolytic streptococci, were found in the cultures, or if guinea-pig inoculation showed the presence of harmful organisms.

No vaccine lymph is issued until it has been stored (below or near freezing point) for at least a month to allow adequate reduction of extraneous organisms under the action of glycerine.

After that time, it is tested for potency and purity and released for general issue as required.

Final purity test

This is a total count of colonies and it is carried out exactly as in the early test. It shows that the extraneous organisms have been greatly reduced in number and in practice it is quite usual to find the lymph sterile at this stage. In Great Britain under the Therapeutic Substances Act, the standard is 'less than 5,000 organisms per cubic centimetre'.

Potency test.—This is carried out on calves. Six 'cups' are tested on each calf and to diminish the chance of working with an unsatisfactory calf (e.g., a calf resistant to vaccinia) the experiment is duplicated, i.e., two calves are used for each set of six 'cups'. The shaved belly of each test calf is marked out into six areas and each area is further divided into two or three, depending on the number of dilutions to be tested. Samples from each of the six 'cups' are diluted to 1/500, and 1/1,500. About five one-inch incisions are made for each dilution. The results are read after 120 hours. A perfect result shows complete vesiculation in all dilutions and in practice the usual result is 'almost complete vesiculation in the 1/1,500 dilution' and complete vesiculation in the others. This calf test was first introduced by Cunningham and then the dilution used was only 1 in 500. The potency having increased, higher dilutions have had to be used for differentiation as seen from figure 3 where the lower half is 1 in 500

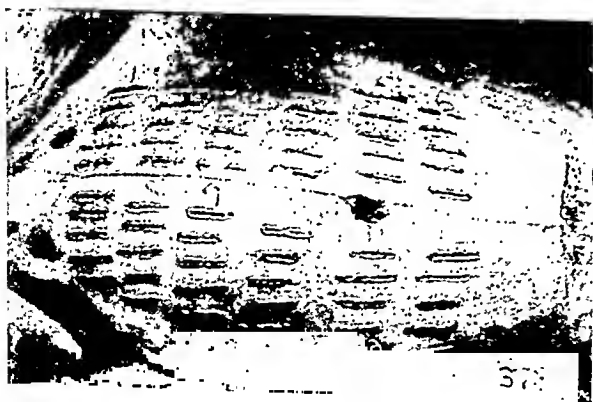


Fig. 3.

and the upper half 1 in 1,500, the vesiculation with the latter is almost continuous.

Less than two vesicles per linear inch in the 1/500 dilution used to lead to rejection. This standard is now applied to the 1/1,500 dilution. In Great Britain, a lymph dilution of 1 in 1,000 must produce the characteristic lesion when applied to the scarified skin of a rabbit or guinea-pig.

Field test

A sample from each 'cup' at this stage is issued for the vaccination of children in the

local Saidapet Range. This provides evidence close at hand of the efficacy and harmlessness of the 'cup' in the event of unsatisfactory results or complaints from other districts and thus gives us a very satisfactory control.

When the 'cup' has been passed for issue, it is filled into tubes as required. One cubic centimetre represents 30 human doses with four insertions each. The dilution is 1 in 7 of the original calf lymph—1 in 5 in the hot weather. The present filling arrangement as devised by King is that lymph is delivered into tubes from a large-barrelled syringe the plunger of which is controlled by a micrometer screw so graduated that one full turn of the stem delivers one-half cubic centimetre of lymph from the nozzle. The tube is then corked and the corked end dipped in melted paraffin. The label of the tube has a distinctive colour depending on the number of doses. Each tube is wrapped in tow and tubes are packed in cardboard boxes according to demands. The contents of each box in tubes and doses is shown on the address label.

The seed

As mentioned above, seed is selected from calves showing particularly good vesiculation. About 5 grammes are removed from the best areas of the selected lesions. This is diluted to 1 in 2½ with 50 per cent glycerine and stored in the cold until required. When it is to be rejuvenated, generally within a few days, it is further diluted to 1 in 5 and a dozen drops are spread on the shaved back of a rabbit. The area is then thoroughly scarified with a matchstick. Seventy-two hours later, the rabbit lymph is removed with a blunt metal spatula after the usual washing and softening, and further material is removed after rubbing a few drops of glycerine solution on the area. The rabbits used are observed for a month before and after operation. Any suspicious illness leads to rejection of the seed, especially anything suggesting the possibility of encephalitis.

The rabbit lymph is diluted to 1 in 5 with glycerine solution and is used at once to vaccinate buffalo-calves. Two first-series buffalo-calves are used for each two strains of rabbit lymph. Thus the first buffalo is vaccinated with one rabbit strain on the anterior part of the belly and with another strain on the posterior part, while in the second buffalo the positions are reversed. The skin is tougher than in cow-calves and a sharp scalpel is used. The incisions are 2 to 3 inches long and about 1½ inches apart, and 30 to 40 incisions are made for each rabbit lymph. The results on the buffaloes are read after 104 hours and lymph is taken from one or both animals according to the appearance within 120 hours of vaccination. The two strains are kept separate, but the yield from the same strain on the two calves may be pooled if both are satisfactory. The lymph is removed, ground and diluted with glycerine

solution and stored as usual. The passage through two second-series buffaloes is carried out in exactly the same way and the yield from these is used as seed to vaccinate calves for the production of stock lymph as required. There is usually an interval of about one week between each of the last few passages.

Notes

1. The slow bactericidal action of the glycerine is aided by the addition of 0.1 per cent clove oil which apparently does not now seriously affect the virus. So experiments are again being done to see whether this can be made the normal practice without real damage to the virus. With the less potent lymph previously used, it was found that clove oil damaged the virus, but it is hoped that this will no longer be the case.

2. While routine production is confined to the cooler months in Madras—September to February inclusive—it has been found by experience that seed lymph stored during the hot weather is not so satisfactory as fresh seed lymph obtained by regular passages during this period.

3. Vaccine lymph rapidly loses its potency at a high temperature. It is, therefore, recommended that supplies from the institute exposed to ordinary temperatures of the Madras Presidency should not be used more than four days after receipt. In Great Britain, under the Therapeutic Substances Regulation, 1927, a statement has to be printed on the label to the effect that unless the lymph is stored at a temperature under 10°C. (50°F.), the potency cannot be guaranteed for more than 7 days.

4. The animals are comfortably housed as seen from figure 4. The area vaccinated is a

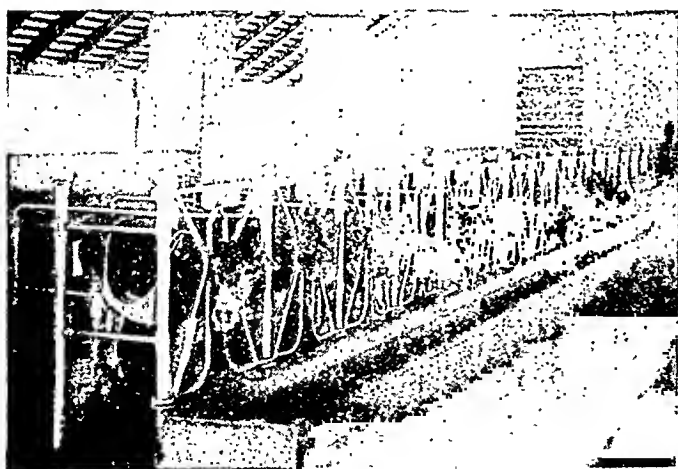


Fig. 4.

comparatively small one so the animals suffer very little from the process. The practice of vaccinating along the flanks as well as the ventrum, as is done in some places, is to be deprecated.

CEYLON HEALTH UNITS*

By W. P. JACOBS, M.D., D.P.H.

Advisory Health Officer to the Department of Medical and Sanitary Services, Ceylon

Introduction

No unusual difficulty is now experienced in planning a suitable public health organization for a municipality. Numerous models are available for study throughout the world. The question is only one of meeting the budget demands.

In rural sections the situation is different. The means of raising revenue are often unsatisfactory; the distances to be traversed are great; communications are frequently bad; and the general educational, financial and sanitary levels are low. On the other hand, rural areas contain the greatest number of people and as they are the main sources of wealth of the world, their sanitary environmental conditions should be promoted.

The establishment of health units in rural and semi-rural areas in Ceylon and India has aroused considerable interest among health workers and the general public. In this article the organization of an official unit in Ceylon is described.

Health units

The health unit scheme presupposes that fundamental public health principles are universally applicable. Local financial and other conditions should be taken into consideration, and the procedures which are followed should be based on common sense and on a recognition of what is useful, reasonable and practicable. The object is to bring to rural areas the benefits of health protection which are now enjoyed by large towns and cities. This end is accomplished by dividing rural areas into suitable districts and introducing therein small but completely trained bodies of workers who remain permanently in the delimited area and undertake all public health problems. Their activities embrace health education, general sanitation, collection, tabulation and study of vital and morbidity statistics, control of preventable endemic and epidemic diseases, vaccination and preventive inoculation, maternity and infant welfare work, school health work, and adult hygiene.

More than 600 of these organizations are now functioning in all parts of the world, namely, Ceylon, India, the Straits Settlements, Siam, China, the Philippines, the South Pacific Islands, Europe, the West Indies, South America, Central America, Mexico, the United States, and Canada.

Ceylon

The island of Ceylon is 20 miles south-east of India. It contains 25,322 square miles and,

* The activities reported in this paper were carried out under the auspices of the Government of Ceylon and the International Health Division of the Rockefeller Foundation.

according to the 1931 census, has a population of 5,312,548. It lies wholly within the tropics (6-10 north latitude) and embraces a wide coastal plain and a narrow band of foothills surrounding a central mountainous area. The predominating race—Sinhalese—are Buddhist in religion; the remaining one and one-half millions are Hindus, Mohammedans and Christians. The principal preventable diseases are malaria, infection by hookworm and other intestinal parasites, enteric fever, dysentery, leprosy, plague and tuberculosis. Cholera and smallpox rarely occur.

In normal times, the country is prosperous and progressive. Large estates of tea, coconut and rubber are the principal sources of wealth.

Ceylon has been in contact with western countries since the 16th century and is well advanced in education. Vernacular and English secondary schools are located throughout the Island, and good colleges are found in Colombo, Kandy and other large towns.

A medical college gives full preparation for local practice, but those entering the public health service must offer, in addition, public health qualifications obtained abroad.

The Director of Medical and Sanitary Services is in charge of all curative and preventive work. Distributed throughout the country are 112 hospitals (9,436 beds) and 603 dispensaries, all staffed by government-employed doctors and apothecaries. There are comparatively few private practitioners, but their number is increasing.

The public health branch has 28 medical officers of health. For the most part, the country is divided into districts each under a medical officer of health whose activities consist of the promotion of sanitation and the control of communicable diseases with the aid of sanitary inspectors. A district medical officer with a large area and a small staff of inspectors can only touch the fringe of the necessary public health work, and in Ceylon this type of work, still necessary under existing conditions in many provinces, is now considered to give inadequate results and is being replaced by health units, as rapidly as facilities permit.

Health unit work, adjusted to local needs, was commenced in Ceylon in 1926. In December 1932, eight health units were in operation embracing 856 square miles and containing 440,000 people. The following data in regard to this work are taken in part from the 1931 report of the Department of Medical and Sanitary Services:

Work and personnel.—The type of work carried out has continued as originally planned and the personnel employed is as follows:—8 medical officers of health, 1 medical officer, 51 sanitary inspectors, 12 public health nurses, 48 midwives, 9 clerks, 8 peons, and 11 orderlies and labourers. A hookworm dispenser was attached to each of the units for varying periods during the latter part of the year. The eighth unit was organized too late in 1931 for its figures to be included.

Births and birth rates.—The births in seven of the

units amounted to 12,702 giving a birth rate of 36.7; as compared with 33.1, the rate for the 35 principal towns of the Island. (Statistical collection in health units is more comparable to the collection in the 35 towns than to the collection in the Island as a whole.)

Deaths and death rates.—The deaths in seven of the units total 7,668 giving a crude death rate of 22.1, as compared with 29.6, the rate for the 35 principal towns of the Island.

Infant mortality.—A total of 1,807 infant deaths occurred in seven of the units, giving an infant mortality rate of 142, as compared with 187 for the 35 principal towns of the Island.

Maternal mortality.—There was a total of 229 deaths among mothers at childbirth in seven of the units, giving a maternal mortality rate of 18, as compared with 31.3 for the 35 principal towns of the Island.

Still-births.—Figures for still-births are available only for the urban areas of the different health units. There has been a total of 86 still-births, giving a still-birth rate of 54, as compared with 73.4, the figure for the 35 principal towns of the Island.

Maternity, infant and pre-school hygiene.—The number of health centres has increased from 22 in 1930 to 35 in 1931. The number of child-welfare clinics held is 1,276 as compared with 843 in 1930. At these centres 489 expectant mothers paid 1,259 visits, as against 136 expectant mothers and 561 visits in 1930; 1,313 infants paid 9,917 visits, as against 892 infants and 6,142 visits in 1930; 1,360 pre-school children paid 8,476 visits, as against 874 pre-school children and 6,193 visits in 1930.

Forty-eight trained midwives attached to the health units made 53,129 ante-natal visits to 8,538 expectant mothers at the rate of 5.8 visits per mother and attended at the delivery of 4,985 mothers, paying them 34,582 post-partum visits at the rate of 6.9 visits per confined case. Eleven public health nurses visited 10,450 homes paying a total of 15,810 visits.

Communicable diseases.—1,746 cases of communicable diseases were reported and 1,727 were investigated; 2,911 doses of anti-typhoid vaccine were administered; 10,670 vaccinations against smallpox were done in six of the units by health unit inspectors. Hookworm treatments amounting to 17,689 persons were carried out in all the units.

School hygiene.—There are 313 schools with a school population of 54,473; of this number 5,669 were medically examined; 4,027, or 70 per cent, were found to be defective with a total of 8,376 defects, or 2.1 defects per defective child; 1,647, or 19 per cent of the defects found, were corrected.

Latrine construction.—135 public latrines in all the units received 8,235 inspections. 172 defects were found and 8 public latrines were newly built during the year.

Latrine construction was carried out in all the units; 71,924 dwellings are provided with 29,886 latrines at the rate of one latrine to 2.4 houses. During the year 1,853 new latrines were constructed, as against 1,713 in 1930, and 1,239 were altered to sanitary type, as against 994 in 1930.

313 schools are provided with 255 latrines, i.e., one latrine to 1.2 schools. During the year 19 schools that were without latrines were provided with them.

Public health education.—Public health education has been carried out by means of 152 lantern lectures, 145 lectures without lantern, 16 cinema lectures, 684 school talks, 1,324 village talks, 215 clinic talks; 4 health and baby weeks reaching an estimated population of 152,000, or 34 per cent of the health unit population; 325 conferences with health unit staffs have been held and training in health habits introduced in 14 schools in the different units.

In addition to these detailed activities, 20,101 houses were surveyed; 1,594 consultations and 123 adult examinations were given; 133 public wells received 2,616 inspections; 197 bakeries, 1,041 tea and coffee boutiques, 194 eating houses, 11 aerated-water manufactories, 66 meat stalls, 83 fish stalls, 174 vegetable stalls, 83 dairies, 234 laundries, 170 cattle sheds, 3 soap manufactories and

94 brick and lime kilns received 80,220 inspections revealing 35,666 defects of which 46 per cent were remedied; 8,099 cattle were inspected and 7,852 passed; 4,381 goats inspected and 4,367 passed; 172 samples of milk were examined, and meat, fish and vegetables were seized as unfit for human consumption on 31 occasions.

This enumeration gives an idea of the scope of work performed in health units and indicates the all-inclusive programme which is carried out. The Director of Medical and Sanitary Services closes this part of the report with these remarks: 'This type of work is now being accepted by the people as the line along which health work in the Island should progress'.

The first health unit, Kalutara Totamune, is used by the department as a training station, and as a consequence has a larger staff and a larger budget. Medical officers of health, public health nurses, midwives and sanitary inspectors now attempt no field work until they have spent an allotted period of time at specified tasks in the health unit organization. Twenty-two public health officials from nine countries have visited the Kalutara Totamune and other units to study the methods in use in Ceylon.

Map.—In order to visualize the complete problem the Island was divided into 63 health unit areas which are indicated by differential colouring on a map. To simplify statistical collection, the existing revenue boundaries were utilized.

Selection of first area.—Considerable care was taken in selecting the first demonstration area. The points which were kept in mind were as follows:—

(1) The leading people should earnestly desire the work. Unless this frame of mind is present or secured, it would hardly be worth while making the attempt. This is probably the most important factor in the whole field of selection.

(2) It is essential that the early co-operation of officials should be secured.

(3) It should be located at a district administrative centre. The work is thus recognized as having received the definite approval of government and as a consequence this establishes it as a government effort.

(4) It should be at or near the seat of the central government in order that the work can be given supervision by higher officers and guided along proper channels, and in order that it can be frequently inspected and visited by officials, and easily accessible as a demonstration to visitors and others who are interested.

(5) It is self-evident that the area should contain the usual health problems of the country. There should be a reasonable amount of prosperity and educational advancement.

(6) It should contain town, village and rural populations. If the first unit embraces all groups, the work can be applied in any part of the country.

(7) It should contain the desired number of people. If groups are too small, the overhead expense is great and the numerical data collected are insufficient for proper statistical analysis.

(8) It should be well connected with roads. A medical officer of health spends most of his time in the field in contact with the people of his area. It should be possible for him to reach them easily and promptly.

(9) It should contain a hospital which will supply medical and surgical treatment for the sick who are found during the survey, and assist in correcting defective children, and in complications of pregnancy.

(10) All organized towns and villages in the area should contribute financially up to their capacity. If

necessary, they should pass laws to enable the medical officer of health to carry out the required work.

(11) The first area should be developed with the idea of utilizing it as a training centre for health unit workers. It is economical to have a training station in the country as it avoids the expense of sending officers away for training and enables them to study the home problems in the home environment.

With one exception, these requirements were met in Ceylon with the selection in 1926 of the revenue area known as the Kalutara Totamune.

It is obvious that in the selection of succeeding areas all the points enumerated above need not be stressed, but a unit should not be established in any community which does not evince an active interest in the subject and show a desire to co-operate in every way. Responsible people of the locality can give the necessary assurances.

It is probably unwise to attempt to interest villagers in serious health work in those sections where there is not a fair degree of prosperity. If a villager has to struggle for his daily bread, and to be content with scanty and mean clothes and primitive shelter, it is not reasonable to expect him to listen to health propaganda of any sort. After his poverty is somewhat reduced, his food and clothing reasonably assured, his fields productive and his house respectable, he will have time and inclination to consider other matters. Consequently remote or backward districts should first receive other fundamental attention.

Area of work

Experience in Ceylon indicates that a population of about 80,000 can be successfully handled by the health unit staff, although a smaller population is preferred in the beginning. The first Ceylon area included representative groups living in small towns and villages and on estates. The people included doctors, lawyers, teachers, priests, government servants, planters, shop-keepers, fishermen, cultivators of village gardens and estate labourers.

Value of hospital and dispensary

The dividing line between curative medicine and public health is not clearly defined. It is true that the functions in certain instances are widely separated and in others closely joined. The tendency is towards a more intimate alliance in health unit work. Hospitals are of assistance in maternity and infancy work and in correcting defects found at school medical inspections. This is feasible in Ceylon inasmuch as the curative work and public health work are under a single direction.

Staff.—The health unit organization consists of a permanent staff of trained workers as follows:—Medical officer of health, public health nurses, midwives, sanitary inspectors, clerk and peon. These are full-time workers with recognized qualifications acceptable to and approved by government. The use of government staff is advantageous as the officers can be transferred readily if circumstances require. As in all types of work the quality of accomplishment depends upon the character of the staff selected.

These workers undertake all the public health activities in the area, but specialists from the central office may be called on to make surveys and give advice. All health units are supervised by a senior staff officer.

Medical officer of health.—In addition to the professional qualifications already mentioned, a medical officer of health should be a competent person with field experience and thoroughly interested in his subject. He directs the health work done in his area and inspects

the work of his subordinate staff with sufficient frequency to keep in touch with all phases of each activity. He is the administrative officer of the organization and uses a motor car for travel.

Public health nurse.—The nurse is frequently referred to as the most important member of the staff. It is certain that in relation to maternal and child-welfare work she is an essential cog in the machine. She must be interested in her work, tactful, sympathetic but forceful in carrying out her duties. She should be well known to the people and able to enter the homes without hindrance. By gaining the confidence of the mothers, she will secure their co-operation and become acquainted with the actual situation in the homes.

Public health nurses should be self-reliant, healthy, not elderly in the beginning, and able to do outdoor work at all seasons. Unlike the hospital nurse who works exclusively indoors, the public health nurse does home visiting, gives home demonstrations, and attends pre-natal and post-natal clinics. She supervises the work of the midwives, and after ten days takes charge of the mother and child, and devotes her energies to keeping them well by home visits and by urging attendance at weekly clinics till the child reaches school age. Her activities include also smallpox vaccination, home demonstrations in the care of minor ailments and assistance in school health work. She lives in the district assigned to her and travels by motor car, rickshaw or hackery (bull and wagon). Young married women as well as single women have been found to be satisfactory public health nurses. Under the present methods a Ceylon public health nurse deals with a population of 8,000 to 10,000, but this number will be altered as the work develops and as more nurses become available.

Ceylon public health nurses are trained 4 years (in general nursing 3 years, in midwifery 6 months, and in public health nursing 6 months).

Midwives.—Like all the staff, the midwives are approved by government after 6 months of successful training. In health unit work they are placed under the immediate supervision of the public health nurse. They locate expectant mothers, and take care of them prior to, during confinement and for ten days thereafter.

One midwife is expected to deal with a population of 4,000 within a radius of 3 miles and to do at least 12 confinements a month. They live in the assigned area and travel on foot. It is desirable that the midwife be married and that the entire family stay with her in the area. The health unit midwife is gradually replacing the untrained woman.

Sanitary inspectors.—Inspectors are trained by government medical officers of health for a period of 6 months. Their work includes control of communicable diseases, inspections of water supplies, houses, dairies, markets, hotels and restaurants, tea kiosks, bakeries, and housing and the promotion of latrine construction. In addition they are trained to do smallpox vaccinations and to give mass hookworm and malaria treatment. Each inspector is required to become well known in his area and to gain the co-operation of the people. As with other members of the staff he works on a programme approved by the medical officer of health, and his activities are frequently visited. An inspector is able to deal with a population of 8,000. He lives in his assigned territory and uses a bicycle for travel.

Office.—An office with necessary clerical staff is located in the area. It frequently happens that a government or municipal building can be secured for an office without pay. Rented buildings are used for the central office, but any other building is supplied by the local population as a part of their co-operation.

The clerk is in government clerical service. He is selected for his ability to type and to deal with correspondence and with forms and reports which reach the office from the field.

Laboratory.—A room at each health unit office is equipped for making simple laboratory examinations of stools, blood and urine. The work is done by the medical officer of health or a trained assistant. Material

requiring more complicated procedure is sent to the central laboratory in Colombo for examination.

Cost.—The cost of the work varies with the scale of pay in operation in a country and of the number of staff employed. The cost should be divided between the central government and the local authority in accordance with arrangements agreed upon in advance. Activities paid for by the local authority are confined to the limits of the area controlled by the local authority.

It is important that the central government, as well as the local authority, contribute towards the work. Very few rural communities in any part of the world will be able to support a competent health programme from the village or town finances. In Ceylon local organized communities are asked to contribute the necessary number of sanitary inspectors and midwives and to continue to pay the cost of scavenging and conservancy. The central government provides the rest and correlates the activities in all units.

All members of the staff whether paid by the local or central government are placed under the control of the medical officer of health of the health unit.

In 1931 the cost to government of operating 7 units was Rs. 2,12,381, or 2.2 per cent of the department's expenditure. The expenditure of the local authorities is not recorded as these expenditures would have occurred if there had been no health unit. A budget for a typical area is appended.

Procedure.—After the area was selected and the staff chosen and located, the following procedure was found suitable.

Educational.—(a) An inaugural public lecture was given by a prominent official. This point should be decided in accordance with local conditions. The publicity gained in a formal public opening is often of great assistance in getting satisfactorily started, but a quiet beginning has advantages.

(b) A series of subsequent lectures were given at various points in the area by the medical officer of health containing detailed information about procedure and describing methods of co-operation.

(c) Steps were taken by the medical officer of health for the formation by the people of local societies to assist in carrying out the work.

(d) A systematic effort was made to enlist the active support of prominent persons including leaders in all phases of local endeavour.

Survey.—A detailed house-to-house survey of the area is made on a special form to secure an accurate understanding of the health needs. The survey is all-inclusive and enables the staff to become acquainted with the people and the area, to find out the general sanitary conditions of the environment and to learn the prevalent diseases.

Activities.—After the survey is finished, the data are analysed and the public health problems so revealed are taken up in the order of their importance.

The entire staff work on a definite pre-arranged programme, prepared in accordance with the problems to be met, the seasons, and the general local conditions. In part their work consists of the following activities:—

Health education by means of press articles, pamphlets, lectures with lanterns and cinemas, village and school talks, individual talks by nurses and sanitary inspectors and exhibits. A small library is developed.

Securing co-operation by enlisting the interest of individuals and organizations and obtaining financial help from individuals; by utilizing existing societies and, if there are none, the organizing of social service and other co-operating bodies.

Promoting sanitation through the development, by experiment and practice, of suitable methods of general sanitation, particularly the control of soil pollution by the use of latrines, inspection of food, markets, eating

places and houses, and the establishment of water supplies and sewage disposal plants.

Controlling communicable diseases by the prevention of cholera, smallpox, chicken-pox, measles, plague, malaria, enteric fever, dysentery, hookworm disease and filariasis; by organizing special treatment campaigns against hookworm, malaria, yaws and leprosy; and collecting morbidity statistics.

Vital statistics, collection, tabulation and study.

Personal hygiene, which is promoted by child-welfare clinics at various centres, home visiting by public health nurses, midwifery service, and medical inspection of school children and correction of defects.

Weekly conferences.—A weekly conference attended by all members of the field staff and presided over by the medical officer of health is held every Saturday morning in the health unit office. At that time each member of the field staff presents his own problems of the week which are discussed and decisions as to the procedures to be followed are arrived at. At this conference advance programmes for the following week are prepared. The conference is useful in maintaining interest by keeping members of the staff informed concerning all phases of the work and is a regular activity in all health units.

Co-operation

Public health work done by compulsion has no sound foundation. A health unit should be able to carry out its work without being compelled to enter prosecutions. Resort to law is the final step. A conviction makes enemies and secures compliance only with the particular item under consideration.

To get lasting results the work must be placed on a co-operative basis which is the foundation of the health unit system. Co-operation is obtained by carefully explaining in lectures and personal conferences to those concerned the objects to be attained and the assistance which may be given in carrying out the programme. Types of co-operation are :

Community.—Social service organizations were formed in the totamune at Kalutara and at Beruwala to assist in promoting the child-welfare work. They continue to function in the original manner. Sub-committees were named for each health centre and a member attends the weekly clinics at the centre, arranges for the distribution of milk to those needing it, and conducts the sewing activity of the little-mother classes. The leagues are supported by private donations, monthly contributions and 'our-day' collections, and their activities are not a charge against the health unit budget. At Beruwala the local league furnishes a building as a centre for holding the weekly well-baby clinic.

Private.—Two public-spirited people rented and furnished two buildings for holding weekly well-baby clinics at two centres. Two other people donated land, building and furniture for operating one clinic. One superintendent provided a good building on his estate on a yearly nominal rent, and one person provided a pump for a public well in a village.

Municipal.—When the health unit includes a self-governing town or village, it is necessary to have an understanding with the local officers. A conference is arranged and after the details are explained, the local authority learns that it loses no power over its employees, but gains considerable help without additional expense. The following rules have been adopted and have proved satisfactory. The local authority agreed to :

(a) Entrust all the municipal health work to the medical officer of health of the health unit.

(b) Pass the necessary regulations and bye-laws to enable the medical officer of health to carry on his work in a satisfactory manner.

(c) Contribute the salary and allowances for the required number of approved sanitary inspectors and midwives.

Objections

In spite of the success attained by health unit work, criticisms of health units have been made by some well-informed and responsible people, but for the most part by those who know nothing of the system. Some of the criticisms are that health units are :—

(a) *A western idea and not suited to the conditions or the people of the east*.—After careful consideration, this does not seem to be a real objection as many western ideas have already been adopted in the east. Furthermore, the statement has been made that in ancient village governments, sanitation was an important item of the administration. If that is true, the health unit only attempts to restore these early usages.

In 1933 this objection lacks force as there are 8 units in operation in Ceylon and several in India, Burma, Siam, the Straits Settlements, Java, the Philippine Islands and other eastern countries. In all these units the adaptation to local conditions were kept in mind and put into practice.

(b) *Too costly*.—It is true that the cost is greater than district work in a similar area, but even so the *per capita* expenditure is less than that usually recognized for carrying out efficient public health work. Although more is paid out, more is received for the outlay. A man must pay more for a silk suit than for a cotton suit as he gets a better article which gives longer and better service. The health unit prefers to accentuate quality of work.

A proposal to introduce health units into the entire area of any state or any country at one time has not been made and is not feasible for numerous reasons. Trained staff is not available; many areas are not suitable for any type of efficient health service; and the people are frequently not prepared to co-operate. Since health units meet the needs better than any other rural health organization, it seems reasonable that they should be established as rapidly as practicable.

(c) *Small in area*.—In a large country a health unit may seem to reach only a small group of people as compared with the total population and as a consequence a large majority of people will thus be deprived of any health service. On the other hand, if the health unit staff should be spread out to reach these other people, the workers would be so

widely scattered that it would not be possible to do any effective health work. As a result no good would accrue to the people in any part of the district.

In health unit work in rural areas, it is possible to carry out intensive activities and thus accomplish definite results. This is usually not feasible in a district plan. Health units act as a stimulus to other areas, set an example of effective work and tend to bring to other health work higher standards of excellence.

The district work in Ceylon has much improved since the advent of health units.

Other criticisms have been offered, but they were mostly of a trivial nature. All real criticisms have ceased when a health unit has been visited and its work given careful study.

Based upon experience health units are suitable for Ceylon and it is the purpose of the government to develop this type of work. Given a fair trial, health units may meet the needs of other states or countries.

APPENDIX I

HEALTH UNIT—PARANAKURU KORALE

Statement of expenditure—January-December, 1931

Central Government

Number	Description	Salaries	Allowances	Total	GRAND TOTAL
	Personal emoluments:	Rs. cts.	Rs. cts.	Rs. cts.	Rs. cts.
1	Medical officer of health	6,615.72	661.52	7,277.24	
1	Clerk	934.58	93.45	1,028.03	
4	Sanitary inspectors	4,539.77	1,024.00	5,563.77	
5	Midwives	1,417.85	1,395.86	2,813.71	
1	Office peon	273.28	29.92	303.20	
1	Labourer	288.80	..	288.80	
1	Labourer for field work	40.50	..	40.50	
1	Field attendant	251.80	23.50	275.30	
					17,590.55
	Other charges:				
	Travelling expenses	2,959.31	
	Transport of stores	55.00	
	Rent	460.00	
	Conservancy charges	36.00	
	Cost of stores	231.70	
	Photographs	25.72	
	Cost of stationery	29.46	
	Cost of drugs	131.80	
	Labourer—field allowance	37.50	
	Sundries	27.03	
	Source of funds, Government	3,993.52
					21,584 07

Statement of expenditure—January-December, 1931
Local Board

Number	Description	Salaries	Allowances	Total	GRAND TOTAL
	Personal emoluments:	Rs. cts.	Rs. cts.	Rs. cts.	Rs. cts.
1	Sanitary inspector	1,039.92	256.00	1,295.92	
1	Midwife	600.00	60.00	660.00	
10	Labourers—Conservancy	2,424.00	..	2,424.00	
7	Labourers—Scavenging including 2 park labourers	1,841.74	..	1,841.74	6,221.66
	Other charges:				
	Travelling allowance to sanitary inspector	240.00	
	Uniform allowance to sanitary inspector	74.28	
	Upkeep of scavenging carts	1,069.59	
	Repairs to latrines	114.42	
	Repairs to slaughter house and cattle pound	53.50	
	Repairs to conservancy carts	55.15	
	Maintenance of markets	346.56	
	Cost of latrine buckets	91.48	
	Cost of disinfectants	278.80	
	Upkeep of cattle sheds and stores	19.58	
	Maintenance of I. D. H.	69.65	
	Supplying meals to I. D. H. patients	102.51	
	Building temporary buildings for I. D. H. camp	44.04	
	Despatching milk samples to Colombo	9.57	
	Wages of labourer employed at I. D. H. camp	7.00	
	Wages of guards at I. D. H. camp	45.20	2,621.33
	Source of funds, local board	8,842.99

Statement of expenditure—January-December, 1931
Village Committee

Number	Description	Amount	Total
		Rs. cts	Rs. cts
	Wages of scavenging and conservancy labourers at Dippitiya, Aranayake, Morantota and Undugoda.	990.00	
	Cost of latrine requisites	15.15	
	Fixing a latrine	51.00	
	Repairs to latrine	35.60	
	Cost of disinfectants	36.50	1,128.25
	Summary	Rs. cts	Rs. cts.
	Government	21,584.07	
	Local board	8,842.99	
	Village committee	1,128.25	31,555.31
	Per capita cost, 60.8 cents.		

Indian Medical Gazette

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THE SYNTHETIC ANTI-MALARIAL COMPOUNDS

THE time may eventually come when all galenicals and natural alkaloids in the world pharmacopœias—or perhaps by that time there may be only one universal pharmacopœia—have been replaced by their synthetic equivalents, or entirely displaced by new and more powerful synthetic drugs. So far we have not gone far along the road towards this ideal—if we accept the chemists' point of view—state of affairs, but a beginning has been made; for example during the last few years a large number of synthetic preparations which closely resemble cocaine have been introduced for local and spinal anaesthesia and now the synthetic quinolin derivatives are making a bid for the quinine market.

For centuries the cinchona alkaloids have held the field, almost unchallenged, in the treatment of malaria. Many specifics have appeared and have enjoyed varying periods of popularity, but the majority of these have contained cinchona alkaloids as their principal ingredient, and if they have not their popularity has been very short-lived. However, very soon after the introduction of plasmochin it became apparent that the privileged position of the cinchona alkaloids was likely to be challenged in the near future. At the time of its introduction it was repeatedly pointed out, both by its originators and by those who used it in the first clinical trials, that plasmochin did not represent the last word in synthetic compounds for the treatment of malaria but was the one that hitherto had given the most promising results of some thousands of closely allied compounds prepared in the I. G. Farbenindustrie laboratories at Elberfeld. The work of selecting from these the compounds that are likely to be efficacious in human malaria is in some ways a task calling for as much ingenuity as did the original preparation of the compounds. It is out of the question to do this testing on man, and plasmodium and hæmoproteus infections in birds have so far presented the best opportunity. Professors Roehl and Kikuth have more than justified this method of selecting these drugs by their successes up to date. Writers who emphasize the disparity between laboratory and field experiments—sometimes in words which suggest that they alone have realized this difference—appear to have forgotten that before a drug can be tested in the field it must go through the processes of selection in the laboratory and then trial under carefully-controlled hospital conditions. The drugs that have been issued by the Elberfeld laboratory

up to the present have had the most conscientious testing as to their safety and their efficacy before they have been allowed to come into the hands of the general medical public. Even then as there are racial and individual variations in the constitutions of human beings it may take many years of very extensive trial before all the possible reactions of man to a drug have been experienced. Few of the new powerful specifics are really fool-proof, and it is essential that in the early stages of our experience with them even field experiments should be very carefully supervised by competent doctors; where this cannot be done, it is better for all concerned that the experiment should not be undertaken.

Plasmoehin was issued to the general medical public about 7 years ago; in some ways it has fallen short of the expectations of its originators, in others it has exceeded them. It was found that in the doses originally advocated it produced toxic, sometimes dangerous and even fatal, symptoms in certain individuals, and that therefore it was necessary to administer it under strict medical supervision. But on the other hand it was found that the original dose advocated was unnecessarily high, that a much smaller dose was almost equally efficacious, and that by the addition of a small quantity of quinine the curative value of this smaller dose of plasmochin could be raised to the maximum level. Then again it was found that plasmochin had little if any effect on the asexual forms of *Plasmodium falciparum*; but on the other hand it was shown that in very small doses it destroyed the sexual forms and that in even more minute doses it sterilized the parasite so that further development did not take place even if this parasite were taken up by a carrier mosquito. From the time that this observation was made plasmochin has attracted the attention of the sanitarian who has seen in it a new weapon. Hitherto it was only possible to break the malaria infection cycle by attacking the mosquito transmitter, because the cinchona alkaloids had no direct effect on the gametocytes, the stage of the parasite that infects mosquitoes. Anti-gametocyte treatment is now a practicable sanitary measure, but it is not a universally-applicable one, any more than is larval control; there are places where one measure is applicable, there are places where the other is applicable, there are a few places where both are applicable, and unfortunately there are probably a much larger number of places where neither is applicable. Larval control has been practised since the time when Ross made his great discovery; it has had its triumphs and its failures. The failures, when properly and honestly reported, have added more to our knowledge of the subject than have the successes. There is still much to be learned about mosquito control, but the malariologist of to-day has so many facts at his disposal that when confronted with

a malaria problem he is in a position to give an opinion as to whether or not some form of mosquito control is likely to be of value, and further to say which particular method should be adopted in the circumstances.

On the other hand effective anti-gametocyte treatment is a new measure which has not yet had a sufficiently long trial to justify any dogmatic opinion. Trials have been carried out and very promising results have been reported; some of these reports have appeared in our pages. On theoretical grounds the main objection to the anti-gametocyte method is that it is a matter of all or nothing.

Many years ago Ross, tackling the malaria transmission problem from a mathematical point of view, concluded that in a given area provided the mosquito population were reduced below a certain level malaria would eventually die out, but that if the mosquito population were above an effective level the introduction of one gametocyte carrier would eventually lead to the infection of the whole community; or in other words that the aim of mosquito control need not be to destroy the last carrier mosquito but only to reduce the mosquito population below the effective level, and on the other hand that the aim in gametocyte control must be to remove the last carrier or the measure would be a failure.

The first part of this conclusion has for many years been accepted as an axiom, and—since complete eradication of the carrier species is usually impossible—on it much of the malaria control throughout the world is based. The second part of the hypothesis nobody has yet satisfactorily refuted on paper, and, in view of the fact that in certain places, such as Punjab villages, where in the inter-epidemic periods the gametocyte-carrier rate falls as low as 0.1 per cent, epidemics occur whenever the carrier-mosquito rate rises above a certain level, and that in endemic areas such attempts as have been made at gametocyte control have been so unsuccessful, it has been tacitly assumed that in this Ross was also correct. The past failures of gametocyte control were obviously due to the ineffectual methods that were used, but now there is an opportunity of testing this hypothesis properly.

The ideal conditions for testing the value of gametocyte control are a heavily malaria-infected community, living in isolation and separated from their nearest neighbours by a distance greater than the range of the carrier mosquitoes in the district, and under a fair degree of discipline. Discipline is a very essential factor as without it a number of persons will evade treatment and the experiment will be vitiated. Now these are very special conditions and it is probably very seldom that they can be complied with, but as we have said it is only in *theory* that this is an all-or-nothing measure, and although Ross's hypothesis has not been disproved it has not yet been proved,

practically, in an endemic area, so that it is possible that an antigametocyte control scheme which falls short of perfection might produce an appreciable effect on the malaria in a community.

An experiment has recently been started in Bengal which consists in attempting to control malaria in a certain area by anti-gametocyte measures. This area covers certainly not more than 20 square miles; if it were completely round (which is the best shape it could be from the point of view of the success of the experiment), the periphery would be nearly 16 miles in extent and $2\frac{1}{2}$ miles the greatest distance any one person would be from this periphery; there is little in the way of natural barriers to prevent free intermixing of the inhabitants with others outside the area, and no measures to restrict movement could possibly be taken; and finally the population is the ordinary rural population of Bengal, under no sort of discipline. Whole-hearted co-operation of the people is expected and will no doubt be obtained in many of the villages, but in a population of 20,000 there are certain to be some who will consider the scheme a government measure designed to annoy them and will refuse to take their plasmodium, or let their children take it. Thus, on the *theoretical premisses* outlined above, the experiment must be a failure. There are however a number of people who think that there is a considerable chance of its being a success. We sincerely hope that they are right, but we are ourselves not prepared to prophesy the result; time will show this. If it is a success we shall have to conclude that the theoretical premisses were wrong, that in anti-gametocyte control it is not a matter of all or nothing, and that an extensive anti-gametocyte campaign can achieve a degree of success even under very unfavourable conditions; on the other hand if it is a failure we shall not know wherein it has failed, whether the failure was due to a large number of persons escaping treatment, whether it was due to the normal interchange of population and the introduction of untreated gametocyte carriers, or whether it was due to the invasion of infected mosquitoes along the relatively very large periphery of the area under experiment, but it will certainly do nothing to prove that anti-gametocyte control in general is a failure as a sanitary measure.

The success of plasmodium as a gametocytocidal drug has overshadowed its more limited success as a schizonticide and as a drug for the treatment of the malarial attack; it was however in this rôle that it made its *début*. In the treatment of benign tertian malaria it scored a very striking success, and the fact that to obtain the maximum effect it is necessary to combine it with quinine does not detract from its value. The relapse rate in benign tertian malaria has always been over 50 per cent, usually about 70 per cent, whatever course of

quinine has been given; plasmochin alone has reduced this to 30 per cent, and combined with quinine—according to Sinton and his colleagues—a cure rate of 91 per cent may be achieved with a single course, even in persistent relapsers. Against the schizonts of malignant tertian it appears to have very little if any action at all. Again its value as a practical personal prophylactic has not been established. About two years ago James, Nicol and Shute staged an experiment to test its prophylactic potentialities but the dosage they used was not a practical one and Swellengrebel and others have since shown that in doses smaller than those James employed, but still too large for daily administration, it has no prophylactic qualities.

About two years ago we were told by someone who had attempted to summarize the literature on plasmochin that there were 400 papers in medical journals on the subject, and as they have been increasing by geometrical progression, it will be safe to estimate that the figure has now reached a thousand. It cannot therefore be said that the medical profession as a whole has neglected this drug or failed to appreciate its advantages and its limitations; the latter have been very clearly defined in a number of papers, and they are scarcely a matter of controversy, but there is still, in India at any rate, a surprising amount of misunderstanding on this subject amongst members of the medical profession and therefore not unnaturally amongst the laity also. Plasmochin is frequently prescribed purely as a curative measure in the treatment of malignant tertian malaria; usually the patient is saved by the fact that quinine is added, but we have heard of cases in which plasmochin alone was given with disastrous results—not brought about by the plasmochin itself but by the untreated malaria infection. The resident in the tropics—more especially the European resident—often considers that it is as unnecessary to consult a doctor when he has malaria as it is when he requires a dose of salts; (we do not admit that he is right in this, though circumstances will often make self-treatment necessary;) with quinine he was fairly safe as the subjective symptoms of overdosage are well known, very obvious and far from pleasant, but this is not the case with plasmochin, and the patient may not associate his symptoms with the drug he is taking. Cases have recently come to our notice where a patient, who has had plasmochin prescribed once by his doctor, has subsequently purchased it, treated himself, and eventually come to hospital with marked cyanosis, dyspnoea and a *Plasmodium falciparum* infection; in other cases the patient has taken plasmochin daily over long periods as a prophylactic measure. The following illustrates what may happen when laymen act without advice:—

A planter living in a malarious district took a tablet of quino-plasmochin (containing 0.01 gramme of

plasmochin) daily for two years as a prophylactic measure; during this time he remained quite free from fever. When he obtained a fresh supply he was given tablets of plasmochin simplex by mistake; these tablets contained 0.02 gramme of plasmochin. He noticed that the tablets were smaller than those he had been taking and proceeded to double the dose, that is, to take two tablets at a time. He then had an attack of malaria, and by way of treatment he decided to take his two tablets three times a day. Thus, in the place of the original 0.01 gramme daily, he was now taking 0.12 gramme of plasmochin, and he continued to do this until he became seriously ill.

The time has passed when it can be said that plasmochin should only be given under hospital conditions. We know that in effective doses it can be given under field conditions, but, as personal idiosyncrasy is far from uncommon, a course should not be prescribed unless the patient is under medical observation, or unless previous experience has shown that with the dosage prescribed the patient is not susceptible.

It is now a little over a year ago that atebirin, another synthetic compound chemically allied to plasmochin, was put on the market. In its action atebirin is much more closely allied to quinine, as it destroys the schizonts of all three species of malarial parasite. The immediate success of this drug was due to the fact that it was issued by the Elberfeld laboratories and that it had already been given a very extensive clinical trial in Germany, England, India, America, the Federated Malay States, and many other countries, from all of which uniformly satisfactory results were reported. It was found to destroy the schizonts of all three species of malarial parasite and to be far more efficacious in the prevention of relapses than quinine; Green at Kuala-Lumpur in a mixed series of 50 cases had no relapses after a seven-days course, and Thonnard-Neumann in Columbia also had a hundred per cent success after a five-days course in the same number of cases. Probably the most striking results were obtained by James and his co-workers in England in the treatment of induced malaria, where with a five-days course he cured patients who had proved entirely refractory to prolonged treatment by quinine. These first reports on atebirin were so complete and so consistently satisfactory that there was little left to be said in praise of the drug and the more recent publications have been concerned mainly with its short-comings. We have received reports of the frequency of relapses following atebirin treatment, but these have been mostly from malaria-endemic areas where the possibility of re-infection was very great. Working with monkeys, we ourselves have found that after an infection has been controlled—that is, kept at a sub-clinical level but not completely eradicated—by treatment or by the animal's natural powers of resistance, it is almost impossible to superimpose a second infection, but if the animal is completely cured by a thorough course of treatment then it is re-infected easily. It is possible that the same

thing occurs in man and that after completely effective atabrin treatment re-infection occurs more readily than after partially effective quinine treatment. On the other hand it is possible that in certain endemic areas, such as Assam and Bengal, the local strain of parasite is more resistant to treatment, as James found with certain Italian strains. We have every reason to believe that the toxicity of atabrin is very low and that it will be possible to give a longer course and larger doses than have been given in most cases up to the present. A monkey weighing 4 kilogrammes will tolerate a dose half the size of that usually prescribed for an adult man, and hitherto few serious symptoms have been attributed to atabrin alone. Some misunderstanding has arisen with regard to the discoloration of the sclerotics by atabrin, which is a yellow dye, and by its excretion in the urine; jaundice and hæmoglobinuria have been reported in such cases. Again, atabrin has a depressing effect on some people and in a few gastric discomfort has been noticed after the standard dose; this has been more frequently observed when it has been combined with plasmochin. Recently, a curious incident occurred in a tea garden in Assam where an experiment of treating the whole force with atabrin and plasmochin was being attempted; about 60 per cent of the coolies reported sick with various symptoms before the treatment was completed. The superintending medical officer of the group of gardens to

which this one belonged lived some miles away and, as the experiment was made during the rains when the roads are almost impassable, he could not supervise the scheme personally nor was he able to investigate the 'incident' personally until some days later; some of the coolies had already been found to be malingering and when he arrived on the scene all the patients had recovered. Unless some serious mistake were made in the dosage, which is very unlikely, the simplest explanation for the incident is that a few coolies had genuine abdominal pains, vomiting, and diarrhoea, which may or may not have been caused by the drugs they were receiving, and that the rest were thrown into a panic by the appearance of so-called jaundice and the dark coloration of the urine. Most of the workers who have reported their experience with atabrin have emphasized the absence of any disagreeable symptoms following its administration, but it is possible that instances of personal idiosyncrasy will be encountered from time to time, and that in the presence of certain pathological conditions it may be advisable to withhold this drug; time and experience alone will settle these points.

As a beginning has now been made the succeeding years may bring forth even more efficacious synthetic drugs for the treatment and prevention of malaria; there is no suggestion that the introduction of atabrin is more than another step along the road that leads to Ehrlich's ideal.

Medical News

'SWINEY' PRIZE FOR WORK ON JURISPRUDENCE

THE Council of the Royal Society of Arts give notice that the next award of the Swiney Prize will be in January 1934, the ninetieth anniversary of the testator's death. Dr. Swiney died in 1844, and in his will he left a sum of money to the Royal Society of Arts for the purpose of presenting a prize, on every fifth anniversary of his death, to the author of the best published work on jurisprudence. The prize is a cup, value £100, and money to the same amount.

The award is made jointly by the Royal Society of Arts and the Royal College of Physicians. The prize is offered alternately for medical and for general jurisprudence. If at any time the joint committee of the Royal Society of Arts and the Royal College of Physicians, which is appointed to submit a book to the adjudicators, is unable to find a work of sufficient merit in the class whose turn it is to receive the award, it is at liberty to recommend a book belonging to the other class.

On the last occasion of the award in 1929 the prize was awarded for medical jurisprudence. It will, therefore, be offered on the present occasion for general jurisprudence.

Any person desiring to submit a work in competition, or to recommend any work for the consideration of the judges should do so by letter, addressed to the Secretary of the Society, John Street, Adelphi, London, W.C.2, not later than 30th November, 1933.

THE FACULTY OF TROPICAL MEDICINE, BENGAL

At the examination for the Diploma of Tropical Medicine (D.T.M. Bengal), held at the Calcutta School of Tropical Medicine in March 1933, the following 33 out of 38 candidates were successful:

Passed with distinction

(In order of merit)

- Sudhangshu Kumar Gangopadhaya, M.B. (Cal.). Awarded the 'Chuni Lal Bose' Gold Medal, 1933; private practitioner.
- Trambaklal Hergovind Trivedi, L.M.P. (U. P.), L.T.M. (Bengal), Sub-Medical Officer in-charge, Laboratory, Government West Hospital, Rajkot.
- Maneck Jamshedji Mehta, M.B.B.S. (Bom.), D.P.H. (Cal.), Officiating 3rd Assistant Port Health Officer, Calcutta.

Passed

- Arjan Singh Man, L.S.M.F. (Punjab), L.T.M. (Bengal), L.M.D., Sub-Assistant Surgeon, Government of India.
- Binoy Krishna Banerji, M.B. (Cal.), private practitioner.
- Manindra Nath Basak, M.B. (Cal.), private practitioner.
- Barendra Nath Basu, L.M.F. (Bengal), L.T.M. (Bengal), Medical Officer, Graham Charitable Dispensary, Darsona, Nadia.
- Phanindra Nath Basu, M.B. (Cal.), private practitioner.
- Rabindra Nath Biswas, M.B. (Cal.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), private practitioner.

- Pankaj Kumar Chatterji, M.B. (Cal.), private practitioner.
 Saroj Kumar Chatterji, M.B. (Cal.), private practitioner.
 Indu Bhushan Chaudhury, M.B.S. (Patna), private practitioner.
 Braja Gopal Choudhuri, M.B. (Cal.), private practitioner.
 Arthur Edward Ray Coombes, Diploma, Medical College, Madras, I.M.D., Assistant Surgeon, Government of India.
 Manohar Lal Dang, L.M.P. (Agra), L.T.M. (Bengal), I.M.D., Sub-Assistant Surgeon, Government of India.
 Dhan Singh, L.S.M.F. (Punjab), I.M.D., Sub-Assistant Surgeon, Government of India.
 Henry Louis Francis, L.M.F. (Bengal), L.T.M. (Bengal), I.M.D., Assistant Surgeon, Government of India.
 Gurkirpal Singh, L.M.P. (Agra), L.T.M. (Bengal), I.M.D., Sub-Assistant Surgeon, Government of India.
 William Lawrence McKenzie, Diploma, Medical College, Madras, I.M.D., Assistant Surgeon, Government of India.
 Sailendra Nath Mukherji, M.B. (Cal.), private practitioner.
 V. Narasimha Moorthy, M.B.S. (Mysore), D.P.H. (Cal.), Health Officer, Mysore State Service.
 Susil Kumer Neogy, M.M.F., M.D. (Cal.), private practitioner.
 Edward Gerald O'Flynn, Licentiate Medical College, Madras, L.T.M. (Bengal), I.M.D. Awarded the first prize in Entomology, Assistant Surgeon, Government of India.
 Gopal Chandra Pattanayak, M.B.S. (Patna), private practitioner.
 Samala Ramakrishna Reddy, L.M. & S. (Osmania Medical College, Hyderabad), Sub-Assistant Surgeon, Osmania Hospital, Hyderabad.
 S. A. F. Shamsul Huda, M.B. (Cal.), D.P.H. (Cal.), private practitioner.
 Narendra Nath Saha, L.M.F. (Bengal), Medical Officer, Barat U. B. Charitable Dispensary, Faridpur.
 Kailash Behari Sahay, M.B. (Cal.), Assistant Surgeon, Government of Bihar and Orissa.
 Jitendra Nath Sen, M.B. (Cal.), Assistant Surgeon, Government of Bihar and Orissa.
 Sachansu Kumar Sen Gupta, L.M.F. (Bengal), private practitioner.
 Ram Narain Sharma, L.S.M.F. (Agra), L.T.M. (Bengal), Medical Officer in-charge, Infectious Diseases Hospital and Public Health Laboratory, Agra (Municipality).
 U. Thant, L.M.P. (Burma), Sub-Assistant Surgeon, Government of Burma.
 Charles Louis Thompson, Diploma, Grant Medical College, Bombay, I.M.D., Assistant Surgeon, Government of India.

THE LICENCE IN TROPICAL MEDICINE

THE classes for this licence commence on 15th July at the Calcutta School of Tropical Medicine. The course lasts for about three months; this period includes the examination which commences on about 7th October.

There are this year a few vacancies, as, in the interests of economy, the various governments have not deputed the usual number of their servants to take the class; doctors wishing to take advantage of this opportunity, which would not occur in ordinary times, are advised to apply as early as possible to the director of the school.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of June 1883, Vol. XVIII, p. 166)

CONSUMPTION has always engaged the medical mind deeply; for to one or other of its forms the death of about one-fifth of the adult population of Great Britain is due; and its treatment has been, from the earliest era of medicine until now, eminently unsatisfactory.

* * * * *

Recent study and research concerning tuberculosis bear upon a larger question, that of the parasitic origin and causation of disease, and if it were once firmly established that tubercular consumption is due to inoculation or infection by a parasite organism, the way would be cleared to the demonstration and belief that many other forms of disease, more especially those with which micro-organisms have been found to be associated, are similarly caused. The germ theory being once placed on a stable footing, treatment, preventive and curative, by germicides would become an imperative necessity, and the only questions remaining for solution would be—what are the most effective germicides for particular varieties of pathogenic organisms, and how can they be most effectively applied in the special circumstances of each disease?

* * * * *

If phthisis is due to a bacillus, destruction of this bacillus outside of the body should prevent its spread, and destruction inside the body thwart its progress. The enemy has accordingly been attacked by a host of germicides conveyed through the blood, or more directly by means of 'naso-oral respirators' through the air tubes; but it has been shown that tubercle is practically extra-vascular, and doubt has been thrown upon the power of the respirators in use to yield a sufficient amount of the drug with which they are charged to be of any practical use.

This subject may therefore also be considered *sub judice*.

Current Topics

Carriers of Enteric.

(Abstracted from the *Lancet*, 11th March, 1933, p. 535)

ENTERIC carriers may be classified according to the duration of the carrier state, and also according to the route of excretion of the specific organisms. It has been shown that, in paratyphoid B infections especially, the incidence of temporary carriers in convalescence is high, and the report therefore lays stress on precautions against the spread of infection during the convalescent period. In some cases the carrier state may set in several months after convalescence, and its occasional intermittency is also a factor which adds to the difficulties of control; intervals of infectivity 'may be

separated by non-infective periods of years'. Most of those who continue to excrete bacilli for six months after the acute attack will continue to do so. Those who still excrete after a year, fortunately a small proportion only, will not clear spontaneously; the carrier state becomes chronic or permanent. The chronic carrier after a known attack of enteric fever is sufficiently dangerous, but in the investigation of an outbreak the history of the illness at least provides a clue to a possible source of infection. More dangerous, because more elusive, is the chronic carrier who has had no known attack or whose carrier state is intermittent. The two main routes of excretion are faecal and urinary; it is also well recognized that bone sinuses, or subcutaneous abscesses, may continue to yield pure cultures

for long periods. The chronic faecal carrier or excretor is 'usually a married woman of 30 years of age or upward'. Female chronic carriers exceed male carriers in the proportion of four or five to one. Children rarely become chronic carriers, but are important agents in dissemination because the attack is so often mild and atypical. Faecal carriers, who are occasionally 'mixed' carriers of *B. typhosus* and *paratyphosus*, are far the most numerous class and may be further subdivided into the biliary carrier (gall-bladder or liver and bile-ducts, or both) and the rare true intestinal carrier. Although chronic cholecystitis, usually but not always associated with gall-stones, has been found in a large proportion of faecal carriers, cases have occurred in which the biliary system could be held blameless, the focus being strictly intestinal. Not only may gall-stones be absent but the gall-bladder may show comparatively slight naked-eye changes such as thickening of the mucosa. Histologically, the most marked change observed by the authors of the report consisted in 'localized and diffuse collections of cells in the mucosa, which are mainly plasma cells and lymphocytes with scanty eosinophiles'. They think there is considerable support for Garbat's view that the gall-bladder in these carriers acts as a 'test-tube containing the bile medium in which the typhoid bacteria propagate without affecting the gall-bladder itself'. Urinary carriers, although less numerous, are clearly more dangerous than faecal carriers. Not only are the opportunities for spreading infection greater, but the organisms occur in large numbers in the urine and not uncommonly in pure culture. The nidus of infection appears to be 'most commonly situated in the kidney or kidney pelvis'. That one kidney only may be infected has been shown by means of ureteral catheterization and the clearance of the carrier state after the removal of the unilateral lesion.

Apart from careful treatment and nursing and the provision of a high caloric diet during the acute and convalescent stages, is it possible to prevent or lessen the possibility of the patient becoming a carrier? Prophylactic inoculation diminishes the incidence of clinical attacks. When attacks do occur in the inoculated they tend to be slight, and it has been held by some that carriers after such modified attacks are less numerous. Others, however, have not been able to confirm this. General anti-enteric inoculation of any population liable to exposure is not practicable in peace-time. But the same measure applied to closed communities such as the staff and inmates of mental hospitals is not only practicable but highly desirable. Professor Browning and his colleagues point out that although this measure be adopted the carrier must still be searched for and treated, since amongst the recently vaccinated massive infection may yet result in an epidemic. It is well known also that the protection afforded by inoculation with T. A. B. tends to wane after a year, and to secure full protection thereafter the process must be repeated. It is advised that in addition to bacteriological evidence of freedom from infection before discharge of a case from hospital, examinations should again be made six to twelve months later, compulsory powers being exercised by all authorities in order to obtain the necessary specimens from convalescents and suspects. In Scotland under the Public Health Regulations, it is possible to notify and to remove compulsorily a carrier, subject to the certificate being renewed every three months. In England powers exist merely to prevent enteric carriers from being concerned in the preparation or handling of food or drink for human consumption. In America regulations for the control of carriers are much more comprehensive and drastic. The authors of the report consider that the existing accommodation, usually an isolation hospital, for the investigation and treatment of carriers involving bacteriological, radiological, urological, and operative procedures is not adequate. This is certainly true of many small fever hospitals, but several of the large institutions already possess, or can readily provide, the necessary facilities.

In the treatment of the chronic faecal carrier chemotherapy, physiotherapy, and the administration of *B. acidophilus*, with a view to changing the reaction of the intestinal flora, alike proved ineffective. Vaccine therapy, including Besredka's oral bile vaccines, produced no better results. Where the gall-bladder is the site of infection cholecystectomy has been successful in terminating the carrier state in 75 per cent of cases. Failures may have been due to the fact that the patients were purely intestinal carriers who cannot be detected with certainty before operation. It seems clear that just as the chronic carrier state in diphtheria is most certainly terminated by the removal of infected tonsils and adenoids, so surgical measures offer by far the best chance of success for the cure of the chronic enteric carrier. In both conditions much expenditure of time and money will be saved when this fact is generally recognized.

The Position To-day of Tuberculin in Treatment

By R. A. YOUNG, M.D., F.R.C.P.

(Abstracted from the *British Medical Journal*, 17th December, 1932, p. 1091)

THE introduction of tuberculin was one of the great tragedies of medical research. Premature in its birth, damaged by the excessive zeal of its earliest exponents, or foster-parents—for Koch himself was cautious in his original claims—it has received the fate of the cripple, at times excessive care, at others neglect. Forty-two years have elapsed since its first introduction, and it remains a baffling and elusive enigma, in spite of an almost incredible amount of investigation, scientific and otherwise. To-day some authorities claim that it is not specific in its effects, and that it should be entirely discarded in treatment. On the other hand, there are enthusiasts who claim a specific and curative action for it and recommend its use widely, while there are others who have used it continuously for many years and are convinced that it has a definite though limited value. The time would therefore seem ripe for a critical and practical review of its effects in treatment. If this discussion could serve to clarify the position, especially to determine which of the three attitudes I have just mentioned is the correct one, then a notable success will have been achieved.

I should like to put forward the following points for discussion:

1. Is tuberculin useful in treatment?
2. If so, what are the indications and contra-indications for its use?
3. What forms is it best to employ?
4. Dosage—spacing and limit of doses.
5. How should it be given?
6. How does it act?

TUBERCULIN IN TREATMENT

It may be worth while to consider briefly certain opinions concerning tuberculin.

(a) It is generally accepted that it is completely innocuous to a healthy non-tuberculous person, even in large doses, while in those who have been infected it produces the well-known tuberculin reaction with its three effects—local, focal, and systemic—in greater or less degree, depending on the form employed and the method of administration. It has been supposed until recently that this reaction is specific, and that it is an allergic phenomenon. Both of these contentions have now been called in question, since other protein substances are said to produce a positive reaction in tuberculous patients, and the skin effects have been stated to be due to a general non-specific hypersensitivity to toxic substances in this disease.

(b) It is significant that its routine use has been greatly restricted in many sanatoriums, and entirely discarded in others; it receives scant mention in most textbooks of medicine and in special manuals on diseases

of the chest. Fishberg, in the latest edition of his well-known textbook, joins the ranks of those who advise against its use; he does so on the grounds that it is not certain that its action is specific, that it is difficult to estimate accurate dosage, especially of different preparations, and that it is altogether wanting in therapeutic effects when given in infinitesimally small doses, and may be decidedly harmful in large amounts.

(c) I have always been much impressed by the fact that, in the so-called surgical localizations of the disease—that is, in glands, bones, joints, and the ocular and genito-urinary systems—tuberculin has a considerable vogue, and that, in these conditions, it is the three well-known preparations of Koch which are chiefly employed, whereas in pulmonary tuberculosis the varieties and modifications of tuberculin which have been advocated are remarkably numerous, extending to more than a hundred. This has always suggested to me that there must be some fundamental difference between medical and surgical tuberculosis, and it is evident that the effects of tuberculin have been disappointing in the strictly medical cases, notably in pulmonary tuberculosis. The fact that so many attempts have been made to modify tuberculin for medical as opposed to surgical use in treatment suggests that it has been found wanting in some respects. On the other hand, I cannot but feel that if it were entirely useless it would have been discarded long ago, and would not be the subject of a serious discussion forty-two years after its introduction. My own experience would lead me to believe that tuberculin has definite therapeutic uses, and that these are considerable in the localized or surgical manifestations, and strictly limited in the pulmonary forms of the disease.

INDICATIONS AND CONTRA-INDICATIONS FOR ITS USE

In cases of pulmonary tuberculosis I have only found tuberculin useful in those patients in whom the disease has progressed satisfactorily towards arrest, but who are left with a small amount of expectoration containing tubercle bacilli. A short course of tuberculin may serve to get rid of the bacilli, to dry up the sputum, or to do both. Such effects alone, if established, would justify its use, since the patients are often enabled to return to their families and to their work without fear and without risk. Many employers will not take back a patient of whom it cannot be certified that the sputum is tubercle-free. Tuberculin has been recommended in chronic cases slow to settle down, of the type described by Inman as 'resting afebrile, ambulant febrile'. I am less sure of its value in such cases, and I think its effects require very careful watching; but it is worth considering. The patient should be kept in bed till it is clear that the tuberculin is not producing any severe reaction, and at the first indication that there is hypersensitiveness to it, administration should be stopped or the dose reduced. I am convinced that tuberculin is of great use in some surgical manifestations, notably in localized genito-urinary tuberculosis, particularly where such localizations coexist with chronic or latent pulmonary tuberculosis and where surgery is impracticable or inadvisable. In localized ocular tuberculosis it can be very helpful, if cautiously used, with the strictest control of dosage, in collaboration with an ophthalmic surgeon.

Tuberculin should not be given in those cases in which there is active, spreading, caseous disease, or recent active 'spread'; it is likely to be harmful by inducing a definite focal reaction, which cannot be controlled, and may be the means of increasing the softening of the caseous areas, or of spreading the disease. It should certainly not be given if there is any degree of continuous, remittent, or intermittent fever. The patient is already receiving more of the toxic products of the bacillus than he can deal with, and any administration of tuberculin is likely to do harm. It is generally recognized that it can only be harmful in any form of miliary tuberculosis, whether this be generalized or local. It should not be given if there is definite albuminuria

except where this is due to renal or vesical tuberculosis, since prolonged administration of tuberculin has been known to be followed by nephritis.

BEST FORMS IN WHICH TO EMPLOY TUBERCULIN

The varieties of tuberculin may be classified as follows:—

1. Filtrates of cultures concentrated, or otherwise modified, especially on glycerin broth media. Of these, Koch's original or old tuberculin is the type.

2. Extracts from the bacillary bodies—Koch's T.O. and T.R.

3. Emulsions of ground-up bacilli—Koch's new tuberculin or B.E. Various processes may be applied before emulsification, as, for example, in Dreyer's diaplyte vaccine, in which the bacilli are treated with formalin and afterwards with acetone, with a view to removing their acid-fast characters.

4. Vaccines made from living attenuated cultures, of which B.C.G. is the type.

It should be recognized that any of these varieties may be made from human, bovine, or other sources. In this connection I may perhaps note a fact which is not generally known, that the Therapeutic Substances Act, 1925, which is concerned with the preparation of many agents employed in treatment, restricts the name 'tuberculin' to the first of these groups, and advises the term 'tubercle vaccine' for any substance obtained directly from the bacterial bodies.

My own experience is limited to the three preparations introduced by Koch—namely, old tuberculin, tuberculin T.R. and B.E. There seems to be agreement on the bacteriological side that the tuberculin reaction does not vary in character with the preparation, though it may differ in degree. Attempts to detoxicate tuberculin or modify its toxic effects seem to succeed only in diminishing or destroying its beneficial effects. Personally I prefer B.E. for most medical purposes; it seems to be easier to control and to cause less severe reactions. In surgical cases, particularly tuberculosis of the epididymis, bladder, and prostate, I, in co-operation with my surgical colleagues, have used T.R. I have generally used the tuberculins or tubercle vaccines prepared from human bacilli, but in some ocular cases I have thought that bovine tuberculin has been effective where the human preparation has failed. It is sometimes recommended to start with the bovine tuberculin and later to transfer to the human preparation.

DOSAGE—SPACING AND LIMIT OF DOSAGE

The question of dosage is a difficult one. Believing as I do that tuberculin can be powerfully toxic and harmful if injudiciously given, I always start with infinitesimal doses in pulmonary cases, and I never increase the dose till it is clear that the patient is immune to the one last given. I aim at avoiding any general reaction, and therefore advise that the temperature be taken regularly for at least the day of injection and one or two days after. I usually begin with 1/500,000 mg., and if there is no reaction from this I give, three or four days later, 1/400,000 mg., and then, at the same intervals, 1/300,000 mg., 1/200,000 mg., 1/100,000 mg., or smaller increases if the patient is sensitive. After this the doses can be more rapidly increased—that is, 1/75,000 mg., 1/60,000 mg., 1/45,000 mg., and so on, but I usually extend the interval to seven days by this time. Provided there is no serious reaction and that there is clinical evidence of improvement, I am prepared to go on slowly increasing the dose at weekly intervals or sometimes at ten-day periods till I reach a dose of 1/500 mg., but I rarely go beyond this. Occasionally, when doses of this amount, or larger, are reached, severe local reactions may occur, with marked local infiltration in and under the skin and even caseation and softening. This need not necessarily interrupt the treatment, but suggests longer intervals or smaller doses. In surgical cases in which there is no pulmonary lesion it is not necessary to start with such small doses, and T.R. may be used

commencing with 1/10,000 mg., and working up by weekly doses to 1/1,000 mg., at which level it may be maintained for long periods.

Preventable Invalidism following Childbirth

By JENNINGS C. LITZENBERG, M.D.

(Abstracted from the *Journal of the American Medical Association*, 19th November, 1932, Vol. 99, No. 21, p. 1740)

THE ultimate welfare of mothers cannot be secured by good care during pregnancy and labour alone. Post-partum oversight is quite as important. The objects of motherhood are not attained by bringing a healthy baby to a living mother; they are completed only when that mother is restored to perfect health. Post-partum care must continue until that end is accomplished, whether it takes two weeks, two months or two years. Thus only can invalidism be avoided. The puerperium is too generally considered at an end with the termination of the lying-in period. It should be thought of as consisting of three periods:

1. *The immediate puerperium*.—This is the lying-in period, ending when involution has progressed far enough to enable the patient to be up and about. Every patient should be told that it takes an additional four or six weeks for her pelvic organs to return to normal. She will then appreciate the necessity of following instructions to be careful.

2. *The intermediate puerperium*.—This is the period of completion of involution. The restoration of all tissues involved in child-bearing to normal should be completed from six to eight weeks post-partum, but, unfortunately, this is frequently not accomplished.

3. *The remote puerperium*.—The period of complete restoration to health ends only when all delayed normal processes and every complication of pregnancy and labour have been entirely eliminated.

Time will not permit a detailed consideration of all the valuable procedures necessary in post-partum care, so discussion must be limited to only a few of the more important and too frequently neglected causes of invalidism following childbirth.

While the puerperium is supposed to be occupied chiefly with normal processes, these are so frequently altered and there are so many abnormal inheritances from gestation and parturition that it is often quite pathologic.

ANÆMIA

Anæmia is a common cause of slow recovery after delivery. Its treatment post-partum begins with prophylaxis at delivery, when the loss of blood must be limited to the smallest possible amount; more than 400 c.cm. is too much, and over 500 c.cm. is excessive. Because bleeding is normal after birth, one is too apt to think that even a considerable loss is unimportant. Measurement is the only way to be certain of the amount of bleeding. This can be done by any one, for it is not difficult. All but a small amount can be collected in a small basin. If you think that your patients are not losing too much blood, measure it—you may be surprised. Too much has been said about the ability of women to live following large losses of blood after delivery. We have been too content with saving the woman's life and not anxious enough about her health and the prevention of invalidism.

If bleeding is kept under 400 c.cm., the first post-partum step has been taken in conserving the mother's future health. The second step is examination of the blood after delivery to detect and treat an unsuspected anæmia. Women may live after tremendous bleeding, but one with a low hæmoglobin and red cell count is greatly handicapped in her restoration to perfect health and strength.

TOXÆMIAS

One of the richest rewards of prenatal care has been the saving of mothers by early discovery and treatment of toxæmias. An equally rich experience will

reward him who follows all his toxic patients for a considerable time, to make sure that there is no remnant of damage to the kidney. This is especially true in those cases in which the disappearance of albumin, casts and hypertension and the return of renal function have been prolonged. Nearly always, when recovery is slow, and even when it has been rather rapid, albumin and casts often appear periodically, which will go undetected and an insidiously developing nephritis may be missed unless the urine of every woman who has had toxæmia is examined frequently and long enough to give assurance that the kidneys have become normal. When recovery from toxæmia is slow, the kidneys have been seriously damaged, are more likely to develop nephritis and will be less able to carry the extra load of another pregnancy or any other condition throwing a severe demand on the kidneys.

DISPLACEMENT OF THE UTERUS

In spite of the fact that some women with retroversion of the uterus have no untoward symptoms, this is a source of invalidism in many more. Various authorities place the incidence of retroversion after delivery at from 20 to 40 per cent. In one thousand of my cases the frequency was 25 per cent. Many of these may be prevented by exercises in bed during the immediate puerperium. Other patients may be cured by simply replacing the uterus at the end of the lying-in period, at which time, whether there has been a displacement or not, the patient should be instructed to take moderate physical exercise, to do the kangaroo walk and how to assume correctly the kneec-chest posture. These, particularly the kangaroo walk, help to maintain the normal position of the uterus and not infrequently cause the retroverted puerperal uterus to return to the anterior position. Beck, when he introduced the 'kangaroo walk', proved, by a large series, each alternate one of whom was given the exercise, that those using it had fewer retroversions. An examination should always be made from four to six weeks post-partum. If, at this time, the retroversion persists in spite of its primary replacement and the physical exercises, the uterus should then be replaced and a carefully fitted pessary adjusted. In my series of one thousand consecutive deliveries, I found approximately one-fourth had retroversions at the end of the intermediate puerperium and that 90 per cent of these were cured by a properly fitted pessary. On the other hand, in a control series of gynaecological cases, not recently delivered, I failed to cure retroversions by the use of the pessary in 95 per cent, malposition recurring as soon as the pessary was removed. I also found that if the adjustment of the pessary was delayed even a short time beyond six weeks after delivery, the percentage of cures dropped rapidly until at the end of three months post-partum, failure was the rule.

NEUROSES

Many neuroses follow delivery, owing to a failure of the physician to appreciate that in the surroundings of modern civilization child-bearing is not always a normal process, often taxing a woman to the limit of her physical and nervous strength. Giving sufficient rest and time for recuperation of the general health, detection and treatment of anæmia and attention to general and mental hygiene, until nervous stability is restored, will avoid neurasthenia and psychosis.

INFECTIONS

Pyelitis and pyelonephritis.—Infections of the urinary tract are peculiarly frequent during pregnancy. Pus in the urine is always a danger signal. It should be eliminated promptly, for it possesses grave possibilities as a focus of infection and is particularly apt to result in chronic nephritis. Every case of infection of the urinary tract must be followed until every last trace of pus in the urine is removed, however long it may take. I have seen patients without any other evidence of infection in whom chronic nephritis developed and who

died because pyelitis of pregnancy was neglected after subsidence of acute symptoms and the patient was not followed to complete elimination of the infection of the urinary tract.

Puerperal infection.—It is not sufficient to treat puerperal infection only until fever, leucocytosis and localized evidence of the acute disease have disappeared, for frequently chronic pelvic and distant lesions are left which are dangerous to health and life. The acute infection, by extension into the immediate neighbourhood of the uterus, frequently leaves chronic consequences from pelvic cellulitis, metritis, salpingitis or peritonitis, and the blood-borne germs attack distant organs, resulting in chronic arthritis, grave cardiac lesions and chronic nephritis.

Chronic cervicitis.—Of the local pelvic lesions, the most common and persistent is chronic cervicitis, which, with its annoying leucorrhœa, follows nearly every case of childbed fever and occurs also in an inordinate number in which there has been no sepsis. Cervicitis is not a trivial lesion, but is a focal infection of far-reaching possibilities. Furthermore, chronic inflammation of the cervix is a dangerous disease, for, by its long-continued irritation, it is potentially a precancerous condition. The foundation of many a cancer is laid at delivery by lacerations with their consequent easy infection and by failure to cure a chronic cervicitis. Therefore, every child-bearing woman should be treated until all evidence of cervicitis has entirely disappeared because: (1) an infected cervix is, with its attendant leucorrhœa, an annoying disease; (2) it is a dangerous focus of infection, the same as the teeth or the tonsils, and (3) it is potentially a precancerous condition, for chronic irritation is the one ætiological factor in cancer about which there is general agreement. Therefore, one's first duty in preventing cancer of the cervix uteri is post-partum care to secure an uninfected, perfectly healed cervix by observation long enough to determine that the cervix heals spontaneously after delivery, and if it does not, to secure healing by local treatments, cauterization or repair of lacerations.

SUMMARY

The ultimate welfare of the parturient woman cannot be secured by good ante-partum and intra-partum care alone, but requires equally good post-partum attention:

1. Meticulous care is necessary during the lying-in period, and careful examination is essential at the end of it to detect and correct any abnormalities.
2. Care consists of, also, prevention of hæmorrhage at delivery and the discovery and treatment of anæmia post-partum.
3. Toxæmias must be followed to the complete eradication of all conditions which may lead to chronic nephritis.
4. Displacements of the uterus must be corrected, for a large percentage can be cured.
5. All infections must be followed to complete cure and elimination of chronic sequelæ as far as is possible.
6. Re-examination must be made at the end of the intermediate puerperium to discover recurrence or occurrence of abnormal conditions.
7. Observation must be continued until the mother is restored to perfect health, however long that may require.
8. If adequate post-partum care is not carried to its ultimate conclusion, the consequences may be grave anæmia, general ill health, nephritis, permanent displacements of the uterus, grave cardiac lesions, neurosis, psychosis, chronic cervicitis, cancer and death.

Is the Increase of Cancer Real or Apparent? A Study Based on the Statistics of Canada

By MADGE THURLOW MACKLIN, M.D.

(Abstracted from the *American Journal of Cancer*, September 1932, No. 5, Vol. XVI, p. 1193)

THE statement is frequently encountered that cancer is rapidly increasing throughout the world, the figures

which are brought forward to support this statement being the death rates from this disease per 100,000 of population. The percentage of total deaths which is attributable to cancer may be higher than it was formerly, but that is not in itself evidence that cancer, as such, is on the increase. A higher percentage of cancer cases may be due to the decrease of other causes of death. The death rates per 100,000 of population, however, are more convincing. Thus in all Canada in 1901 the death rate from cancer per 100,000 of population was 46.8; in the next two decades it had risen to 75 per 100,000 of the population, an increase of 62 per cent.

Is the Increase a Real One? This greater frequency has been said by some to be more apparent than real; by others it has been held to be an actual increase.

Various arguments are put forward by those who do not admit a real increase. In the first place, they state that the age of death has been raised, so that more people now live to the cancer age than formerly. In this connection they point to the great saving in lives of infants by social and medical agencies, so that they may live to the age at which cancer will develop. Secondly, there is put forward the idea that diagnosis is much better to-day than it was twenty years ago, so that more cases of cancer are diagnosed than was possible at that time. In the third place, vital statistics are increasingly accurate, another factor which tends to increase the number of deaths attributed to cancer. A fourth argument, which is really a part of the two preceding ones, might be presented, namely, that many more persons are attended by physicians to-day than was the case in 1901. With each year each of these factors operates in such a manner as to enhance still further the cancer death rate. Thus each year sees more infant welfare work undertaken, and a lowering of the death rate in the early years of life. Each year sees a progressively higher percentage of well trained personnel in the medical profession. Each year sees a spreading of medical attendance to a greater percentage of the population and to more and more outlying districts, with the result that statistics are becoming more and more reliable. For these reasons we should expect a steady increase of registered deaths from cancer, and from 1921, when the rate was 75, to 1929, the latest year for which Canadian statistics are available, this expectation has been fulfilled, for the rate has steadily risen until it was 90 per 100,000 for all Canada. If only the registration area of Canada as it was in 1921 be considered, the rate is 93.9 for 1929.

There are observations, also, which lead us to the conclusion that the increase in cancer is more apparent than real. Thus, for example, in 1928 Prince Edward Island had a cancer rate of 114, while Saskatchewan had a rate of only 55, or less than half that of the former province. When, however, we consider the age of the population in the two provinces, we see that in the one with the high cancer rate, 31.5 per cent of the inhabitants were over forty as contrasted with 19.6 per cent in the province with the low cancer rate; also that 13.3 per cent were over sixty in the former as compared with 4 per cent over sixty in the latter. While these percentages are based upon the 1921 census, and do not actually represent the percentages in 1928, nevertheless they indicate the tendency for a population with a high percentage of old people to show a much higher cancer rate than a population made up largely of pioneer families, in which the average age is much lower.

We may visualize mankind as walking over a bridge which spans the river of death. Along its length and width are many trap-doors, through which the unwary traveller may drop into the dark-flowing stream beneath. As the trap-door of infant mortality opens far less frequently than it did before; as the trap-door of yellow fever is practically shut; as the trap-doors of malaria and typhoid and smallpox open but once where they formerly opened a score of times, we find that the troop of people is not nearly so thinned out by the

time the middle of the bridge is reached as in years gone by. Even in the last half of the bridge, the trap-doors that once sprang open with alacrity, now move rustily on their hinges, and the throng which formerly dropped from sight through their hungry mouths now moves over them almost unaware of their existence. But it is a law imposed upon all those who start upon that journey, that they shall never reach the far side. At some time they must leave the crowd and sink into the river. Some of them almost finish the span, and the further they go, the fewer are the trap-doors to betray their footsteps; but at the end, although they are few, they are wide and long, and those who avoided the pitfalls farther back, now drop from sight through fewer doors, that yawn more widely.

Much has been done to lengthen the time which anyone may spend upon the bridge of life. In 1901 the average age of death in Canada was 31; in 1921 it was 38.5. If we exclude all those dying under 5, the average age of death was 49.5 in 1901, and 53.2 in 1921. In 1901 the death rate per 1,000 was 15; in 1921 it was 10.6. We must all die of something, and it is inevitable, as we eliminate one cause of death after another, that we increase the death rate from the causes that remain, for while we may increase the length of life, we do not decrease the certainty of death.

SUMMARY

Cancer is increasing, and it is increasing particularly in the age group over sixty. The reason for its increase is not that it is occurring at progressively younger ages, or attacking larger percentages of the younger population. Despite its increase, deaths are fewer from all causes now than they were. We have won more ground from the ravages of infectious disease than we have lost to those disorders which are dependent upon inherent qualities in the chemical and physical make-up of the individuals. Cancer is increasing because, by preventive methods, there has been created a larger population to grow old; and having grown old, they are kept from dying of those ills from which they formerly suffered. With each increase in the warfare against preventable diseases, there will be an increase in the ravages from cancer, for with each victory there is created a greater available population to die from that disease.

These conclusions are based upon the statistics of Canada. There is strong ground for believing that a similar analysis of the statistics of any other country would lead to the same conclusions. It is true that there may be racial differences in immunity to cancer, but the conclusion here reached will probably prove universal, namely that excellent public health measures and high cancer rates are inseparable, at least for the present. Those who point to the low cancer rates existing among primitive peoples, and who state that cancer is a disease of modern civilization, neglect to call attention to the fact that preventive medicine is itself a triumph of modern civilization.

Removal of the Spleen

By THE RT. HON. LORD MOYNIHAN OF LEEDS

(Abstracted from the *British Medical Journal*,

15th October, 1932, p. 701)

FUNCTIONS OF THE SPLEEN

THE functions of the spleen are not fully understood. Its activities may be grouped in relation to four separate systems.

The hæmopoietic system.—In embryonic life red cells and leucocytes are manufactured here—a return to this function is seen in the leukaemias and in infections in adult life. The Malpighian bodies give rise to leucocytes, and the endothelial cells of the splenic pulp may, under certain circumstances, proliferate and be thrown off into the circulation. It has been suggested that the spleen secretes a hormone which acts on the bone marrow; a rapid anaemia occurs after splenectomy, and

it is possible that this is due to the absence of such a hormone. An intraperitoneal injection of splenic extract in such a case has been shown to cause an increase in the red cells and in hæmoglobin. A substance which restrains the red cells has been supposed to be present, and its absence after splenectomy held to be the cause of the leucocytosis which constantly occurs.

The reticulo-endothelial system.—The spleen is the most important single member of this system. The pulp cells are capable of taking up foreign particles circulating in the blood stream, effete red cells, and perhaps also blood platelets and circulating organisms. Broken-down red cells are carried, probably in endothelial cells, to the Kupffer cells of the liver. Organisms such as the malaria parasite and *Spirochæta pallida* extracted from the blood may be stored in the spleen. The pulp cells have a further function in combating infections by the manufacture of immunizing substances, and it is for this reason that the spleen is constantly enlarged during the course of generalized infections; a lowered resistance to infections is one of the (theoretical) after-results.

The digestive system.—The volume of the spleen varies during the day, an increase occurring during the three or four hours after a meal. It may be that there is some connection between the variation in the size of the spleen and the leucocytosis which occurs during digestion.

The sympathetic-endocrine system.—The sympathetic nervous connections of the spleen are very intimate, and it has been shown that the injection of splenic extracts causes a contraction in smooth muscle. A connection has been suggested between the spleen, the thyroid, and the thymus glands.

INDICATIONS FOR REMOVAL OF THE SPLEEN

Rupture or laceration of the spleen.—Rupture of the normal spleen without injury has been recorded. This is a very uncommon type of lesion, and no explanation of it has been put forward. A series of thirteen cases has been collected, nine of which recovered after operation. Cases due to injury are far more common. There are cases where massive bleeding takes place immediately after the accident; the patient does not recover from the original shock, and death takes place in a very short time. Such cases are due to a tearing of the splenic vessels at the hilum of the organ, or to its actual avulsion. After laceration of the spleen the patient recovers from the initial shock of the injury, and signs due to internal hæmorrhage then make their speedy appearance. In a few cases the initial loss of blood is small, and symptoms of hæmorrhage are not observed until a second effusion of blood occurs. Operation must be undertaken as soon as the diagnosis is made, and the spleen should be removed. Splenectomy gives good results, a recent series showing a recovery rate of 93 per cent.

Movable spleen.—This condition is met with either as part of a general visceroptosis or when the phrenocolic ligament is unduly long. Attacks of severe and sudden pain may be experienced. A case is recorded where a movable spleen lying in the pelvis became twisted; the swelling which resulted caused impaction and intestinal obstruction owing to pressure on the rectum. In most cases relief can be obtained from a well-fitting belt, but in others an operation may have to be performed. As a rule fixation, though possible, is not so satisfactory as removal, which has little or no mortality and is followed by no appreciable disability.

Torsion.—Torsion may occur in a freely movable spleen. The blood supply is cut off, the organ threatens to become gangrenous, and a general peritonitis may result. Relief of the strangulation, and fixation of the spleen have been advocated, but removal of the spleen will probably be necessary in most cases.

Prolapse of the spleen.—Some of the earliest cases in the literature refer to removal of the spleen for prolapse, and the operation appears to have been

followed by recovery in most cases. This must be a rare accident even in war injuries, and splenectomy would only be called for in those cases in which the spleen was badly lacerated or infected. In other cases the spleen would be preserved.

Malaria.—Enlargement of the spleen may be a danger or a discomfort to its owner on account of liability to rupture from trivial injuries. The removal of the spleen may make the disease more amenable to treatment, and so help to cure it. The spleen may be mobile or firmly fixed; if the former, removal is simple and safe; if the latter, it is difficult and dangerous. The mortality is approximately 5 per cent in the former and 75 per cent in the latter condition.

Splenic anæmia.—It is time for the title 'Banti's disease' to be dropped. In Banti's own description I can hardly recognize conditions with which experience in this country has made me familiar. Splenic anæmia is a condition in which the spleen is enlarged, anæmia develops, hæmorrhages are common, the liver undergoes changes resulting at last in atrophy of considerable degree, and ascites is present. It is a continuously progressive disease, and in the absence of surgical relief is invariably fatal. Operation is the one opportunity of saving life. Its danger is directly dependent upon the stage which the disease has reached. In earlier stages the spleen is not greatly increased in size, anæmia is slight, and when the abdomen is opened the spleen is found to have few adhesions, none of them of great density. In later stages anæmia may be profound, the spleen gigantic, and adhesions of such character that their division seems at first almost impossible. In one case I had to remove a piece of the diaphragm, as a condition of cohesion rather than adhesion was present; a gap about two inches long was left in the diaphragm, but closure presented only slight difficulty, and the patient recovered.

There are few, if indeed there are any, operations in surgery which require such careful preparation of the patient. If the spleen is gigantic its size must be reduced by deep x-ray treatment, or preferably by the application of radium. In a few weeks a spleen which seems to fill the abdomen, and to show great salience, is reduced so much that only a slight projection is felt below the left costal margin. Anæmia, which may be profound, is always present, and is especially severe after any form of hæmorrhage; I have had many patients whose red cells did not number two million to the c.mm. Anæmia responds readily and rapidly to transfusion of blood, which may be repeated several times; on two occasions I have given blood five times before removing the spleen. When the general and local conditions are thus improved the difficulties of the operation are not, of course, reduced, but its dangers are much lessened. My mortality is between 6 and 7 per cent, and I attribute this to the care of the patient before operation. There is no hurry as a rule, and a couple of months may well be spent in making the patient safe for surgery.

The immediate mortality of splenectomy in this condition varies according to the stage of the disease and the competence of the operator; the technical difficulties are never, or rarely, overcome without great patience and resource. Bleeding from adhesions must be stopped by pressure with hot large swabs packed into the wound as tightly as possible. The average death rate in skilled hands is approximately 12 per cent. But in the late cases operation does not entirely free the patient from risks. Three of my patients have suffered from hæmatemesis some months or years afterwards, and on two occasions had to be admitted to hospital for transfusion; one of these patients has suffered from hæmatemesis on three occasions. This very disappointing experience makes it clear that operation must be practised at the earliest possible moment. Even in late stages, however, the recovery of the patient is often most remarkable. When the liver is found to be shrunken and hard, when ascites is present, and the outlook apparently almost hopeless, improvement begins

and is steadily maintained, and the patient finally appears to recover completely. There is no doubt that regeneration of liver cells in such cases must be considerable. On one occasion only have I had to tap the abdomen to remove fluid after splenectomy.

In general, it may be observed that success in this operation depends upon two factors: a careful preparation of the patient by the usual methods, especially by blood transfusion, and a reduction of the size of the spleen by application of x-rays or radium; the surgical outlook may so be considerably improved. Except in cases of splenic anæmia, the technical difficulties of the operation are inconsiderable.

Anæsthesia in Tropical Surgery

By C. GRANTHAM-HILL, M.B. (Camb.)

(Abstracted from the *Lancet*, 11th February, 1933, p. 295)

THE difficulty of obtaining good general anæsthesia for surgical operations has always been one of the constant trials of medical work in the tropics. This difficulty is particularly marked in a country such as the Anglo-Egyptian Sudan, in which there are great variations of temperature and humidity, a shortage of experienced medical staff, and a backward and primitive race supplying the majority of the patients. There is, amongst native Sudanese patients, an almost universal dread of losing consciousness under an anæsthetic, a dread compounded of fear of the unknown and a belief that the soul actually leaves the body and may have difficulty in finding it again. There is sometimes also a tincture of doubt as to what mutilation may be in store for the unconscious and helpless patient. The relief with which the information that an operation can be performed without loss of consciousness and without pain is received by such patients contributes greatly to that hopeful outlook which is of such enormous value in the treatment of the African native.

The technical, as apart from the psychological, difficulties of general anæsthesia may be summarized as follows:—

Chloroform, the most dependable of available anæsthetics, is nevertheless dangerous in unskilled hands, and few native medical officers become really dependable in its use. Further, its toxic effect in prolonged anæsthesia is a very real danger, particularly in view of the commonness of hepatic and renal deficiencies in tropical patients.

Ether is very unreliable owing to the great variation in its rate of evaporation following atmospheric changes. It loses bulk rapidly in hot weather, and is apt to explode. Its use needs considerable skill, especially when in combination with chloroform, for the relative strength of the two drugs is continually changing as the ether evaporates. Closed ether appliances seldom survive the climate for more than a few months, on account of the loss of elasticity of the rubber bags or connections. Ether readily causes bronchial irritation in hot, dry weather. The most useful mode of administration is by the rectum mixed with olive oil.

Nitrous oxide.—Both nitrous oxide and oxygen are impossibly expensive, as they have to be obtained from Europe, and the cylinders lose half their contents in transit.

Ethyl chloride is definitely dangerous unless given in measured quantity from a rubber bag, which rapidly loses elasticity.

Avertin has the very grave objection that skilled attention is needed for at least half an hour before operation, and often for 24 hours after it. It is therefore almost ruled out as a routine anæsthetic in the primitive conditions of nursing found in most parts of this country.

The solution of many of these difficulties has been found to lie in the increasing use of local and spinal anæsthesia; the following are the most striking of the many advantages:

(1) The minimum of shock with the maximum of relaxation.

(2) The almost complete absence of post-anæsthetic vomiting. This is of great value both from a physical and a psychological aspect. The patient usually sleeps well, and can take fluids and solid diet much earlier than after general anæsthesia.

(3) Preparatory and after-treatment are simplified. Many cases can be admitted and sent home on the day of operation, thus economizing beds.

(4) One skilled assistant the less is needed.

(5) The co-operation of the patient during the operation is often of great assistance—*e.g.*, a timely cough in locating a hernial sac and the movement of fingers in a tendon suture.

These advantages are, of course, familiar to all surgeons, but work at a distance from the refinements of skilled assistance and nursing lends them such added value as to warrant the emphasis used.

SPINAL ANÆSTHESIA IN ABDOMINAL OPERATIONS

Spinal anæsthesia is the anæsthesia of choice for major abdominal operations on patients who are not profoundly shocked, cachectic, or very old; in other words, for those who are reasonably good 'risks', and can tolerate the inevitable drop in blood pressure. After considerable experience of stovaine, novocain, and spinocaine, we have found neocaine, given by the method described by Koster and Kasman, the most reliable. Over 200 operations have been done under this anæsthetic in the Khartoum and Omdurman Hospitals without any untoward event referable to the drug, and with uniformly satisfactory results. Briefly, the method used is as follows:—

After a preliminary injection of morphia, the interval between the first and second, or second and third lumbar vertebræ is punctured with a fine needle and a quantity of cerebro-spinal fluid is drawn off and mixed with the crystalline neocaine in the glass ampoule in which it is supplied. The solution is then injected slowly through the needle which has been left in place.

For an adult of average weight: 10 mg. of neocaine in 4 c.cm. of fluid give anæsthesia up to the umbilicus; 15 mg. of neocaine in 6 c.cm. of fluid give anæsthesia up to the costal margin; 20 mg. of neocaine in 8 c.cm. of fluid give anæsthesia up to the clavicle.

Immediately after injection the patient is placed in the Trendelenburg position to counteract the cerebral anæmia which follows the invariable drop in blood pressure, and the operation may start within five minutes. Complete anæsthesia lasts for about an hour; if the operation is not completed within this time, novocain may be injected into the peritoneal edges, or a little chloroform given. If there is nausea or retching the head of the table is still further lowered and, if they persist, ephedrine is injected, though this is not often needed. After return to the ward, the head should be kept low until the pulse has recovered its volume. No cases of headache have occurred in this series. This is attributed to the use of a fine needle. The following case illustrates some of the advantages of this form of anæsthetic.

A male native, aged 35, was admitted with a history of sudden onset two hours previously of epigastric pain of an agonizing character, with vomiting and collapse. For two years previously there had been intermittent pain when the stomach was empty. There was board-like rigidity of the upper abdomen, a subnormal temperature, and a pulse-rate of 80, the pulse being of fair volume.

A preparatory injection of morphia, gr. $\frac{1}{4}$, had little effect upon the pain, but 15 mg. of neocaine in 6 c.cm. of cerebro-spinal fluid intrathecally produced complete relief from pain and a flaccid abdomen in five minutes. The patient retched once or twice while the abdomen was being opened, but subsequently went to sleep; a perforation in the posterior wall of the duodenum was closed, and a gastro-jejunostomy was performed under advantageous circumstances. Except for some paralytic

ileus on the second and third days, the patient made an uneventful recovery.

A constant feature in abdominal cases thus anæsthetized is the contracted state of the intestines (except where there is paralytic or obstructive ileus); the abdominal contents not required can be packed away with ease, thus facilitating intra-abdominal manipulations.

LOCAL ANÆSTHESIA IN ABDOMINAL OPERATIONS

In abdominal work local anæsthesia is most useful: (1) in operations not entailing much handling of viscera—*e.g.*, straightforward appendicectomies, colostomy, ventral hernia; (2) in cases where, owing to shock or debility, the patient is a doubtful risk under spinal or local anæsthesia; and (3) in infants. The technique, in outline, consists in:—

(1) Infiltrating the line of the incision by sub- or intra-cuticular injection of 1 per cent novocain, made up with fresh adrenaline, 5 drops to the fluid ounce.

(2) Blocking the cutaneous nerves by a zone of infiltration into the muscle layers, particularly in the neighbourhood of the nerves (intercostal, ilio-hypo-

(3) Anæsthetizing the peritoneum. This is best done after exposure of the transversalis fascia, or posterior sheath of the rectus, when novocain can be injected beneath it, in contact with the peritoneum.

Novocain injected into the mesentery will usually relieve pain due to manipulation of viscera.

The quantity required is usually between 1 and 2 fluid ounces of the 1 per cent solution, but more can be used without danger provided that: fresh, unboiled adrenaline solution is added in the strength mentioned; and care is taken that no appreciable quantity is injected directly into a vein.

A native boy of 9 was admitted with a history of colicky pain in the abdomen, beginning with vomiting 12 hours previously. Examination showed a tumour just above the umbilicus and visible small gut peristalsis. There was faecal vomiting and collapse. After an injection of morphia and local infiltration with 1 per cent novocain, a right paramedian incision allowed a 12-in. intussusception of the jejunum to be delivered and reduced by manipulation. The intussusception had started at a tumour of the gut wall the size of a walnut; this (a lymphosarcoma) was resected, and an end-to-end anastomosis was done at a subsequent operation under a spinal anæsthetic.

GENERAL OPERATIONS

The following notes indicate the general lines of the procedure used.

Abscess.—Many of the smaller types of abscess, and particularly cold abscesses, can be opened almost painlessly through an incision previously injected intracutaneously with 1 per cent novocain. Subcutaneous injections should not be used, as the solution will either enter the abscess cavity, where it will be ineffective, or will be forced into the surrounding zone of hyperæmia, where introduction will be painful and possibly dangerous.

Amputations.—The fingers and toes are easily removed after encircling them with a band of hypodermic injection, a little novocain being introduced more deeply over the line of the nerves. The same method serves for removing ingrowing toe-nails and for opening whitlows, but in the latter case care should be taken not to cause venous congestion by injecting too much of the solution, or pain will result.

For amputating limbs, in addition to the encircling subcutaneous injection, the nerves must be blocked by injecting a considerable quantity of novocain into their neighbourhood or, where practicable (as in the upper arm), by exposing them and injecting the trunks under direct vision. This method is extremely valuable in the emergency amputation of crushed limbs.

Inguinal hernia.—Hernia offers one of the easiest and most useful opportunities for local anæsthesia. After subcutaneous or intracuticular injection of the line of

incision, the needle is introduced at a point about 2 cm. internal to the anterior superior spine and is carried deep to the fascia of the external oblique, and the ilio-inguinal and ilio-hypogastric nerves are blocked with 4 or 5 c.cm. of anæsthetic. Deep injections can then be made round the internal ring, to anæsthetize the peritoneum and cord, or the neck of the sac and genital branch of the genito-crural nerve can be injected after the inguinal canal has been opened.

Hydrocele and varicocele.—These are easily dealt with by (1) injecting the line of incision as described, and (2) blocking the genital branch of the genito-crural and sympathetic nerves by picking up the cord between the fingers and introducing 3 or 4 c.cm. of solution into it.

Tumours of the lower jaw and tongue.—Local anæsthesia here has the enormous advantage of the collaboration of the patient in spitting up blood which would otherwise find its way into the lungs. A preliminary tracheotomy is unnecessary, and the anæsthetist's intrusions are obviated. For the lower jaw one or both inferior dental nerves are blocked by injection of 3 or 4 c.cm. of novocain into the neighbourhood of the nerves as they lie near the lingula on the inner surface of the mandible, the needle being introduced in line with the opposite canine and following the plane of the biting surface of the teeth until the lingula is felt. A hypodermic encircling injection is then made into the face, enclosing the area of the operation.

Hemi-section of the tongue.—This can conveniently be carried out, if the anterior two-thirds only are involved, by blocking both inferior dental nerves as described above, and also the lingual nerves as they lie on the floor of the mouth.

Madura.—The use of local anæsthesia should be confined to the removal of very small early madura, which can be encircled by a hypodermic injection without risk of penetrating the growth. If the injection penetrates, as it easily may in larger growths, the consequent œdema makes differentiation difficult. The larger growths also need a bloodless field only obtainable with a tourniquet, for which general or spinal anæsthesia is necessary.

Skin grafts.—Thiersch grafts are conveniently cut by encircling the area from which the graft is to be taken with a weal of subcuticular injection of 1 per cent novocain.

A native man, 50 years of age, entered hospital with a tumour of three months' duration projecting from the external surface of the left mandible. There was an indurated ulcer on the external alveolus opposite the premolars, and the submaxillary lymphatic glands were enlarged but soft. After removal of the teeth, morphia and hyoscine were injected and the left inferior dental nerve blocked inside the mouth with 5 c.cm. of 1 per cent novocain. A line of subcuticular injection of the same solution was next described round the tumour, and carried forward to the symphysis mentis. Through an incision carried back from the angle of the mouth, and dividing to include the skin adherent to the tumour, the whole mass, together with the body of the mandible from the symphysis to the angle, was removed in one piece. The divided skin and mucosa were sutured. Healing occurred by first intention, and the glands gradually subsided. The growth proved to be an epithelioma invading the bone.

SPINAL ANÆSTHESIA IN GENITO-URINARY OPERATIONS

Spinal anæsthesia is of inestimable value in *suprapubic prostatectomy* on account of (a) the excellent relaxation, (b) the absence of shock and toxic action on the kidneys, and (c) the almost total absence of hæmorrhage due to the fall in blood pressure. If the removal is not done under direct vision and the prostate bed sutured, care must be taken that reactionary hæmorrhage does not follow the rise in blood pressure some hours after operation. In many cases it is advisable

to anticipate this by exerting pressure on the prostate bed by means of a hæmostatic bag or gauze plug attached to a catheter in the urethra to which a weight can be suspended.

LOCAL ANÆSTHESIA IN GENITO-URINARY OPERATIONS

Ligature of hæmorrhoids.—Piles can be satisfactorily ligated under local anæsthesia, which gives better relaxation of the sphincter than even deep general anæsthesia; the relaxation appears to last longer with the former method, thus giving freedom from pain after operation. The anus is first encircled by a weal of subcutaneous 1 per cent novocain. One finger is then placed in the anal canal, and under its direction a needle is passed, at intervals of about 2 cm., deeply into the sphincters and under the anal mucosa, 2 c.cm. being injected at each spot. The needle point should be kept moving so as to avoid injecting into the veins. After a few minutes the sphincter will be found relaxed, and the operation can proceed.

Suprapubic cystotomy.—Either for the removal of calculi, or as a preliminary to prostatectomy, suprapubic cystotomy is easily performed under local anæsthesia provided that novocain can be injected via the urethra. It is particularly useful in the case so often already on the edge of uræmia, in which there has been long-standing prostatic obstruction. Ten to twenty cubic centimetres of 5 per cent novocain with two drops of adrenaline are first injected into the bladder with an ordinary urethral syringe, the bulbar urethra being massaged to pass the solution upwards. A hypodermic weal is next formed along the line of the suprapubic incision with 1 per cent novocain, a little being also introduced beneath the rectus sheath. The bladder is then exposed in the usual way, a further injection being made into the thickness of its wall before it is opened. If the peritoneum has to be stripped up, as is sometimes the case in contracted bladders, it should first be infiltrated with novocain.

Fistula in ano.—This is treated as for hæmorrhoids.

LOCAL ANÆSTHESIA IN EYE, NOSE, AND THROAT OPERATIONS

Many operations on eye, nose, and throat are so commonly performed under a local anæsthetic that no comments are needed. The following, however, may be less familiar.

Trichiasis.—The operation of splitting the inverted lid margin and tarsal plate and inserting into the cleft an epithelial graft from the lip can be done under local anæsthesia as follows. The conjunctival sac is anæsthetized by instillation of cocaine drops at half-hourly intervals thrice in the ward, morphia being given with the third. On the table, the lid affected is injected with 2-3 c.cm. of 1 per cent novocain, a little being also introduced with a fine needle into the conjunctiva of the under side of the lid. The lip which is to provide the graft will also need an injection of 2 or 3 c.cm.

Enucleation of the eye.—This can be done painlessly by injecting 1 or 2 c.cm. of 1 per cent novocain to the neighbourhood of the otic ganglion, the needle being passed inwards along the outer wall of the orbit for a distance of 2 cm. and then a little towards the nasal side. A little solid cocaine may also be placed in the conjunctival sac and, if there is blepharospasm, the lids should be injected with novocain.

CONCLUSIONS

It is emphasized that no originality is claimed for any of the procedures or technique described, all of which are fully described in textbooks of local anæsthesia. Of these, the writer has found Farr's to be the most useful. The intention has been to give a brief account of the type of case found most suitable for spinal and local anæsthesia in a general surgical practice in the tropics.

Reviews

THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY. Volume I:—Anatomy and Physiology. Volume II:—The Technique of Clinical Medicine. New York and London: D. Appleton and Company, 1932. Volume I. Pp. lix plus 1273. Illustrated. Volume II. Pp. xxxiii plus 984. Illustrated. Available from Messrs. Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 37-8 per volume. (The set is to be completed in twelve volumes and Index.)

THE reviewer received these imposing volumes with a sense of grievance, that in these hard times another huge medical encyclopædia should be thrust on to the market. However, he was very rapidly placated, and he is now completely converted to the point of view of the conceivers of this extremely ambitious undertaking, which is no less than an attempt to provide the general practitioner with all the information he can possibly want on any subject connected with his profession, in one set of volumes; we must wish the publishers and editors every success in their venture.

Volume I

This volume is appropriately devoted to anatomy and physiology. In the 676 pages apportioned to anatomy, although there are enough cold anatomical facts recorded to get the student through the average anatomy examination, the physiological and the practical aspects of the subject have been kept in view so that the pages provide excellent reading for the practising surgeon and physician. In the same way the physiological portion, which comprises the other half of the book, really deals with pathological physiology and many of the sections would have supplied excellent introductory chapters to a textbook on pathology. One cannot discuss the individual contributions or contributors, but the latter are all men of established positions in the best-known teaching institutions in the United States. Before concluding our remarks on this volume we must mention the very excellent anatomical illustrations; in these all the various structures are differentiated by the use of colour, and in clarity these 'figures' compare favourably with those in any textbook on anatomy that we have seen.

Volume II

This volume is entitled 'The Technique of General Medicine'. It is a book of nearly a thousand pages, so that the various writers cannot complain that they have had insufficient room to do justice to their subjects. They have, however, not been profligate with their space and in the sections we have had time to peruse we have found each item of technique very completely described without any padding in the form of descriptions of obsolete methods. In the title the word 'medicine' is used not in the general sense but in the special sense, medicine as distinct from surgery; the volume might have been entitled 'Clinical' or 'Diagnostic Methods', though it is more comprehensive than books with these titles usually are. For example, in the chapter on 'The Blood', which covers 160 pages and contains as many words as the average monograph on the subject, there are paragraphs on the origin and development of blood cells, on the histology of the organs of hæmopoiesis, on the functions of the blood cells, on the normal blood count, and on the blood count in different diseases, as well as on the methods by which the various counts and estimations are actually made. An earlier chapter is devoted to physical diagnosis. There are chapters on the bacteriological and serological diagnosis of separate diseases and groups of diseases, on the technique used in the diagnosis of allergic diseases, diseases of metabolism, endocrine diseases, and so forth, on genito-urological diagnosis, on

neurological examinations, and on examination of the eyes, of the ears, nose and throat, and of the mouth. This is of course not a comprehensive list, but it will, we hope, give some idea of the wide scope of this volume.

CHRONIC RHEUMATISM AND THE PRE-RHEUMATIC STATE.—By J. D. Hindley-Smith, M.A. (Camb.), M.R.C.S. (Eng.), L.R.C.P. (Lond.). London: H. K. Lewis and Co., Ltd., 1932. Pp. x plus 144. Price, 5s. 6d.

ON receiving a small book on an everyday medical problem, one's first desire is to classify it. There are a number of classes into which a book of this nature may be placed. It may represent a chapter from a textbook on general medicine by a master of the subject; such books are popular with practitioners nowadays, as they are light and easily slipped into the pocket. It may be a book by a specialist who has a particular theory he wishes to advocate, which is sound enough to be accepted by a section of the profession, but not sufficiently orthodox to be put into a textbook. Finally, there is the book written by the faddist whose views are so unorthodox that no journal will print them. In this instance the name of the publishers is a guarantee that the book is not of the last-named class. We are afraid, however, that we must place it in the second class. Nevertheless, the book contains a well-balanced discussion on the subject, and the author does not over-emphasize his own particular views. Streptococcal vaccines and local treatment of the foci of infection are his sheet anchors, but not to the exclusion of other treatment, such as hydrotherapy. He is quite positive in his statement that the primary focus is *always* in the nasopharynx, but he did not make it clear why he considers that the foci in the bowel and teeth are secondary. He has a very intriguing theory about host-parasite adjustment and/or allergy, which he does not pursue to the extent of boring his readers; he is content to stir their imagination. The author has a curious prejudice against following the usual British custom of italicizing the scientific names of bacteria, and, when quoting another writer who does follow this harmless practice, he goes to the extent of denying all responsibility by inserting 'The italics are his'. A stimulating little book, printed on most excellent paper.

L. E. N.

A TEXTBOOK OF MEDICAL JURISPRUDENCE AND TOXICOLOGY.—By Rai Bahadur J. P. Modi, L.R.C.P. & S. (Edn.), L.F.P.S. (Glasgow). Fourth Edition. Calcutta: Butterworth and Co. (India), Ltd., 1932. Pp. x plus 1003, with 83 illustrations. Price, Rs. 15.

THE present edition of this book is considerably enlarged, and has been revised throughout, with the addition of a considerable number of good original illustrations. New sections have been added on blood-grouping tests, tetra-ethyl lead, carbon tetrachloride, medinal, luminal, naphthalene, trinitrotoluene and quinine. Almost every aspect of medico-legal importance has been dealt with. The book is, on the whole, well written and well arranged, and contains a lot of information which should prove quite useful to students and practitioners in India. There are certain deficiencies which might be remedied in the next edition with advantage. For instance, the ages at which the epiphyses of long bones unite in India are considerably earlier than those in European countries; in some cases this ranges between one and four years earlier. Some work on this subject has been done by Dr. Galstaun, Radiologist, Medical College Hospitals, Calcutta, and could have been included in the book. Again the use of sodium thiosulphate in combating poisoning by arsenic is recognized by all authorities and might be with benefit added in the next edition.

D. A.

A COMPENDIUM OF THE PHARMACOPŒIAS AND FORMULARIES.—By C. J. S. Thompson, M.B.E. Seventh Edition. London: John Bale, Sons and Danielsson, Ltd., 1933. Pp. ix plus 381. Price, 10s. 6d.

THE latest edition of this compendium is, of course, based on the new British Pharmacopœia. It is rather fuller than the average compendium and contains invaluable information on a variety of matters, directly or remotely connected with dispensing and prescribing. There are synopses of thirteen different foreign pharmacopœias, lists of useful non-pharmacopœial prescriptions, of stock mixtures, and of poisons and antidotes, tables of comparative weights and measures, of solubilities, and of boiling and melting points, translations of French, German, Italian and Spanish words commonly used in prescriptions, Latin words and their abbreviations, and so forth; the contents list covers two and a half pages.

The information given is all useful, as far as we can judge it is accurate, and in most cases it is up to date. An exception is the technique that is advocated for the examination of blood for malarial parasites; for this they have given a method suggested by Manson in 1894.

The volume is a handy one, and can easily be slipped into the pocket. We can strongly recommend this compendium to dispensers and practitioners in this country.

THE THEORY AND PRACTICE OF MASSAGE AND MEDICAL GYMNASTICS.—By B. M. Goodall-Copestake. Fifth Edition. London: H. K. Lewis and Co., Ltd., 1933. Pp. xx plus 332, with 118 illustrations (including 22 plates). Price, 12s. 6d.

THIS book, prepared by a teacher of the Chartered Society of Massage and Medical Gymnastics, is an admirable textbook. It embraces the complete syllabus of the Society in the theory of massage and of medical gymnastics, and contains a full description of the surgical and medical conditions treated by massage and movements, with details of their application. The illustrations are clear, helpful, and up to date.

Students in training will find this book very useful; furthermore, those members of the Chartered Society of Massage and Medical Gymnastics in distant parts of the world, where they can get no immediate advice or help, now have a book to which they can turn for reference, and which will keep the aims of the Society and the theory of their work constantly fresh in their minds.

P. B.

ANNALS OF THE PICKETT-THOMSON RESEARCH LABORATORY. Vol. VIII. (The Common Cold.) By D. and R. Thomson. London: Baillière, Tindall and Cox, 1932. Pp. xxiv plus 738, with 51 plates. Price, 63s.

'It is all very well for you doctors to spend your lives investigating rare and interesting diseases, but what you ought to do is to come down to earth and find a cure for the common cold'. This remark, or one of similar purport, has been made to the reviewer not less often than once a month for the last ten years or so, by some normally intelligent layman. Others have probably suffered in the same way. At last he has a formidable answer, and he will no longer have to submit weakly to this platitude. This volume of 738 large quarto pages, of roughly half a million words, and 51 full-sized plates consists of brief résumés of the more important papers that have been written on this subject of the common cold. Every aspect of the subject has been dealt with, and in each section the authors have given their own views. These are always well considered and well expressed, and those who have only a short time at their disposal will do well to seek out these paragraphs. The authors' criticisms are usually very shrewd, as for example when they say that two of the present fashions in medical research are to put everything down to filtrable viruses,

and to carry out a small number of examinations on a very large number of persons, instead of, as they themselves prefer, carrying out a large number of examinations on a much smaller number of persons. However, there is something to be said for fashions, provided that they are not taken too seriously. Every disease of which the causative organism is not known will now be a filtrable-virus disease until it has been proved not to be; it is one way of tackling problems.

The reviewer feels that he must again express his gratitude to the authors of these annals and the patrons of the laboratory from which they are issued each year. They are really splendid gifts to the research workers of the world. Every library attached to a research institution should possess the complete set; fortunately, the back numbers are still available, and the cost to the purchaser is only a fraction of the sum the volumes must have cost to produce.

L. E. N.

FUNGUS DISEASES: A CLINICO-MYCOLOGICAL TEXT.—By H. P. Jacobson, M.D. London: Baillière, Tindall and Cox, 1932. Pp. 317, with 153 illustrations. Price, 3s.

THIS book is a useful compilation of the existing knowledge on mycology in so far as it affects human pathology.

Like many scientific publications from America this book gives the impression that all the most important work on mycology has been done in the United States and that the rest of the world has given a little assistance here and there. This idea is fully borne out in the lists of references at the end of each section. The number of errors in typesetting is rather greater than usual, and amongst the proper names one finds Manson called Mason. In one place treatment is advised as follows '..... beginning with a dosage of five drops Tid.....'. This appears to be a hypercontraction of *Ter in die* and it is hoped this word is only another printer's error and not a new Americanism.

The author has made a new departure in having two introductions written by different people and we feel that the second one might have been better omitted for it begins as follows:—

'The American medical world greets with enthusiasm the appearance of this most important book on "Mycology" by Dr. Henry P. Jacobson'.

This is a rather surprising statement, as it must have been written before the American medical world had the opportunity of greeting the book. It is followed by a rambling statement in which certain outstanding discoveries in medicine are mentioned, practically none of which have anything to do with mycology and appear to have been chosen at random; this remarkable introduction concludes with the following sentence. 'Gratitude is due to him not only from the physicians of both hemispheres but from the countless patients whose suffering will be alleviated by his scientific contribution to all humanity'.

Extravagant language of this kind is likely to prejudice a reader against a book rather than to encourage him in the anticipation of the perusal of a valuable contribution to science.

P. A. M.

AN EMPIRE PROBLEM: THE HOUSE AND VILLAGE IN THE TROPICS.—By D. B. Blacklock, M.D. The University Press of Liverpool. London: Hodder and Stoughton, Ltd., 1932. Pp. 100. Price, 3s. 6d.

THE sub-title of this small volume is somewhat misleading for although health problems of the house and village occupy a considerable portion of the book essays on tropical medicine, the economic importance of maintaining an adequate supply of properly trained medical men in our tropical possessions, and other kindred subjects are also dealt with.

Broadly speaking the lesson conveyed by the book is that disease would be lessened by better housing, sanitation, and pure water supplies in tropical villages.

There is nothing very original in this point of view and many places even in the British Isles could still be found where the same principles might be applied with advantage, as well as in any other part of the Empire.

Although he sets out to discuss the various problems from an empire point of view, the author's horizon appears to have been limited by the West African bush, to judge from the examples of tropical hygiene and pathology that he gives to point his arguments.

AIDS TO DISPENSING.—By A. O. Bentley, Ph.C. Second Edition. London: Baillière, Tindall and Cox, 1933. Pp. vii plus 204, with 10 figures in the text. Price, 3s. 6d.

The second edition of 'Aids to Dispensing' is another welcome addition to the now famous 'Students' Aid Series'. Dispensing is an important art which calls for manual dexterity as well as theoretical knowledge. In this small treatise, the essential requirements of the students going up for their pharmacy examinations are set forth systematically, with special reference to the practical details, and it therefore should be particularly useful.

In India, the importance of having qualified dispensers in pharmacies has not yet been fully appreciated. The present state of affairs is bound to improve in view of the recommendations of the Drugs Enquiry Committee appointed by the Government of India in 1930-31. Books of this type will then be in great demand by students who would like to take up dispensing as a career.

R. N. C.

AIDS TO MATERIA MEDICA.—By G. H. Newns, M.B., B.S. (Lond.), M.R.C.P. (Lond.). London: Baillière, Tindall and Cox, 1933. Pp. vii plus 141. Price, 3s. 6d.

Books of the Students' Aid Series have already gained a good deal of popularity amongst the student community. The reason is not far to seek. Students all over the world want a rapid turnover of the whole subject during the time of the examinations and books of this series have served their purpose efficiently. The recent addition to the series is 'Aids to Materia Medica' by Dr. G. H. Newns and, like its predecessors, this book is likely to be popular.

The book is divided into three parts; part I deals with the common drugs and their composition, preparations, and pharmacological actions; part II deals with the materia medica of inorganic and organic substances including synthetic compounds; sections are included on gland extracts, vaccines, and anti-toxins; and part III consists of a list of preparations, followed by a grouping of drugs according to their pharmacological actions. This part is likely to prove of supreme utility to students. The two appendices are no less useful and contain a valuable list of drugs having doses less than 1 grain.

R. N. C.

DIABETES MELLITUS OR EROTOMANIA.—By M. Vijaya-Raghavulu, B.A., M.B. & C.M. First Edition. Madras: Published by the Gautama Printing Office, 1933. Pp. xiii plus 239. Illustrated. Price, Rs. 5.

We were inclined to believe that the strange title of this book was designed solely to attract the attention of the curious, until we encountered this paragraph in the book itself.

'The one invariable condition I found during my thirty-three years' practice in every diabetic subject of over forty years of age is *excessive sexual indulgence in men and frequent child-birth in women*. One and all of the subjects have evidently excessive internal secretion of testis and ovary and are consequently chronic *erotomaniacs*. To draw pointed attention to the cause, I venture to call the disease *Erotomania* as well'.

The least that one expected from the author was that he would come forward with facts and figures in justification of views which depart radically, as he says,

from those commonly held; yet, beyond a repetition of the same statement in a somewhat more exaggerated form, we find nothing in the book which goes to support it. No further comment on such a book is necessary.

ANATOMY (CATECHISM SERIES). PART II: LOWER EXTREMITY. Fourth Edition, Revised and Enlarged, by Charles R. Whittaker, F.R.C.S.E., F.R.S.E. Edinburgh: E. and S. Livingstone. Pp. 68. Price, 1s. 6d., and postage 2d.

This small book of the Catechism Series deals with the inferior extremity, chiefly on a regional basis, subdividing it into seven parts, viz, the buttock, the popliteal fossa, the thigh, the leg, the sole of the foot, joints and the ossification of bones. The new nomenclature has been chiefly adopted, the old names being mentioned in parenthesis. The relations of the main blood vessels have been nicely shown in tabular form. The unimportant anatomical details have been left out, but the structures and regions of surgical importance, such as the femoral triangle, adductor canal, and the popliteal fossa, have been carefully dealt with in the form of questions and answers. The book will be extremely useful to students for quick revision of the subjects during their examination.

N. P.

OTHER BOOKS RECEIVED

A New Theory of Cancer and its Treatment.—By C. F. Marshall, M.Sc., M.D., F.R.C.S. Published by John Wright and Sons, Ltd., Bristol. Price, 3s. 6d.

First Studies on the Health and Growth of the Bengalee Students.—By A. N. Chatterjee, M.B., B.S. Published by the Calcutta University. Price, not stated.

Selected Addresses.—By V. B. Green-Armytage, M.D., F.R.C.P., F.C.O.G., Lieut.-Col., I.M.S. Price, Rs. 2.

Annual Reports

ABSTRACT OF THE REPORT OF THE LEAGUE OF NATIONS REGIONAL HEALTH CONFERENCE AT CAPE TOWN, SOUTH AFRICA, 15TH TO 25TH NOVEMBER, 1932, BY MAJOR-GENERAL J. D. GRAHAM, C.B., C.I.E., K.H.S., I.M.S. (PUBLIC HEALTH COMMISSIONER WITH THE GOVERNMENT OF INDIA, AND DELEGATE FOR BRITISH INDIA), AND OF THE REPORT OF THE SAME CONFERENCE ISSUED IN THE QUARTERLY BULLETIN OF THE HEALTH ORGANIZATION OF THE LEAGUE OF NATIONS. VOL. II, EXTRACT NO. 1.

The following countries, to the administrations of which invitations had been sent, were represented:

Angola,
Basutoland,
Bechuanaland Protectorate
and Swaziland,
British India,
Kenya,
Gold Coast,
Mozambique,

Nigeria,
Northern Rhodesia,
Southern Rhodesia,
South West Africa,
Tanganyika,
Uganda,
Union of South Africa,
Zanzibar.

The Rockefeller Foundation was also represented.

The main subject dealt with at this Conference was the possibility of the spread of yellow fever by means of motor vehicles and aeroplanes. The general discussion is full of interest but is amply covered by the conclusions which are given below. In addition the statement by General Graham, the representative of the Government of India, is given *in extenso*. He outlined the history of the attitude taken by the Indian Government towards the possible risk of the

introduction of yellow fever into India, laying special stress upon the immense population at risk and upon the difficulty which would be experienced in the eradication of the disease if once established. He pointed out that an aedes survey undertaken at some of the major ports in India before the war revealed a high aedes infestation, and that, owing to the condition of life in large Indian towns, aedes control is exceedingly difficult. Observations published concerning the possibility of protracted incubation periods of the disease in man and of protracted infectivity periods gave further cause for anxiety.

For the above reasons, and to meet the point of view of the Government of India, General Graham stated that the Office International d'Hygiène Publique had altered Article 48 of the Sanitary Air Convention to read as in the present draft, and had recorded their views of its interpretation in their *procès-verbaux*.

The Government of India meantime felt that, although anxious to avoid interference with the ratification of the Sanitary Air Convention, yet, in the light of available information and in accordance with present conditions, prohibition of air traffic from yellow fever areas to susceptible areas was the only reliable safeguard.

General Graham stated that the discussion at this Conference will be of great assistance to the Government of India as defining the concerted action to be taken by the governments of susceptible countries in Africa; but, in view of the possibility of the introduction of yellow fever into the Sudan or East Africa, owing to a break-down in measures taken in any one link of the chain from west to east, the position still required further consideration before the future action of the Government of India could be decided upon.

Conclusions.

(1) None of the fundamental observations upon which public health control of yellow fever is based have been disturbed by recent knowledge. Although under exceptional conditions the incubation period in man may be protracted or the infectivity period may be prolonged, and although experimentally a wider range of dispersal of the mosquito vector has been shown to be possible, yet, for practical purposes, public health control of yellow fever can be based upon the observations that yellow fever is transmitted from actual human cases only in the first three days of the attack, that the incubation period of new cases does not exceed six days, that the agent of transmission is a domestic mosquito which remains in, or in the immediate vicinity of, the house where it has fed, and that the insect, after feeding upon an infected case, must survive for twelve days before it can transmit the virus to another person.

(2) The mouse-brain virus protection test may be accepted as specific for yellow fever.

(3) Large areas in the countries of central, eastern and southern Africa, believed at present to be free from yellow fever infection, must be regarded as infectible.

(4) It is of obvious importance that immediate action be taken to ascertain the position with respect to the presence of the disease, unsuspected, in endemic form, and also to the susceptibility of the population to the disease, in those African countries in which yellow fever has so far been unknown. In these enquiries, the Government of the Anglo-Egyptian Sudan, not represented at this Conference, should be invited to participate. It is satisfactory to record that action recommended in this section is already envisaged in French Equatorial Africa, as well as in Angola; that protection test surveys have already been commenced in the Belgian Congo, and that arrangements are now in progress for similar surveys to be carried out in the Union of South Africa, Bechuanaland Protectorate, South West Africa, Mozambique, Southern Rhodesia, Northern Rhodesia, Tanganyika, Kenya, Uganda and Zanzibar.

(5) Steps should be taken for the provision of equipment and for the training of staff at laboratories in Africa, appropriately selected and situated, where necessary yellow fever work can be carried out after the termination of the detailed work covering many parts of Africa, which is now being undertaken by the Rockefeller Foundation. Such work would include the performance of protection tests and of protective vaccination.

(6) For the purposes of paragraphs 4 and 5 above, the importation of fixed mouse-brain yellow fever virus should be permitted in laboratories in Africa, under Government authority and control.

(7) The co-operation of the Rockefeller Foundation in the establishment of laboratories for yellow fever control advocated in paragraphs 4, 5 and 6 above, in the manner suggested by Dr. Sawyer, is particularly welcome.

(8) The action taken by the British Government in providing facilities in England for protective vaccination against yellow fever deserves attention, and it is hoped that other administrations concerned with public health work in Africa will provide similar facilities at those laboratories where yellow fever work is being carried out or is being projected.

(9) The risk that infection with yellow fever from west to east may spread from village to village by the opening up of new trade and motor routes should be taken into account. It is hoped that the present position along such routes may be determined by protection test surveys of the population, and that the position thereafter may be reviewed from time to time by re-surveys. This slow method of spread of the disease may ultimately prove more capable of breaking down our defences than the more rapid spread which can result directly from modern fast means of transport. In this connection it is suggested that the excellent motor routes which now exist from the French Cameroons across French Equatorial Africa and the northern section of the Belgian Congo need to be considered in connection with risk of infection to the Anglo-Egyptian Sudan and to Uganda.

(10) Although the possibility exists of transport of infected mosquitoes by air, rail or road, it is considered that the greatest risk, or at least the more difficult risk to avoid, consists of the transport of a person during the incubation period of the disease.

(11) It is agreed that the Governments of African countries should be advised forthwith to accept and ratify the International Sanitary Convention for Aerial Navigation, 1932.

(12) The systematic communication of new facts in regard to yellow fever in Africa to the Office International d'Hygiène Publique in Paris, for consideration by its Yellow Fever Commission, is provided for by the above Convention, and this system should be utilized as fully as possible.

(13) Yellow fever control, as now carried out in the West African countries, is an important factor for the protection of neighbouring countries from yellow fever infection, and it is important that these measures should be continued and their efficiency augmented. Special stress is laid upon the provision of pipe-borne water supplies, active destruction of aedes in towns and villages, and the segregation of the non-indigenous population in residential areas in which effective aedes control can be maintained.

(14) The Health Departments of African countries believed at present to be free from yellow fever infection should obtain more information concerning aedes infestation than is now available, and should introduce, or make more effective, measures for the control of aedes in those centres at which risk of introduction of yellow fever infection is specially to be apprehended.

Annex 1 consists of a long address by Dr. W. A. Sawyer, the Rockefeller Foundation representative, in which he dealt with the recent advances in yellow fever

pathology, and as these have already been given in our April issue in the abstract of the Annual Report of the Rockefeller Foundation they are omitted here. His statements about the barriers against the spread of yellow fever are, however, of considerable interest to India so this portion of his statement has been abstracted.

How great is the danger of the extension of yellow fever from West Africa to East Africa and from there to the Orient? It seems highly probable that both these regions are infectible. The mosquito vector, *Aedes aegypti*, is present. Indian and Javanese strains of this species have been shown to be capable of transmitting yellow fever to monkeys by biting. Natives of India are susceptible, for Indian labourers in South America have died of the disease. Daniel Blair reported on an epidemic in British Guiana in 1856 and gave the numbers of cases and deaths in natives of India. The mortality among the Indians was about the same as that among seamen and resident Europeans. Whether the East African negroes would differ from those in West Africa in the degree of their susceptibility to infection with yellow fever or their power to resist the effects of the disease we do not know. The hope that parts of the Orient in which dengue is prevalent might be non-infectible because of cross-immunity between yellow fever and dengue has been taken away by the recent observation of Stefanopoulo and Callinicos that the sera of eleven persons who had recovered from dengue would not protect mice against yellow fever virus.

Since East Africa and parts of South Africa are in all probability infectible, it is important to study the barriers which have protected these regions from invasion during past centuries. The ocean barrier was highly inefficient in the days of the slave trade, when sailing vessels with larva-infected water-butts carried yellow fever back and forth between Africa and the Americas. The voyages by the longer and less frequented route around to the eastern coast of Africa do not seem to have transplanted the infection. Even now the coast-wise shipping may be a factor in the waves of yellow fever which occasionally occur in West Africa, and involve a number of ports. The ocean barrier needs constantly to be reinforced by the rigid suppression of mosquito breeding in ports and on ships.

The barrier to the north of the infected region is a wide band of arid country with a small population, including Mauritania and the Sahara Desert. This barrier has been highly effective against the spread of yellow fever northward. The disease does not infrequently approaches the southern fringe of this arid belt, and Johnson has concluded, on the basis of the studies and experience in Nigeria, that the dry northern country is infectible and able to maintain the infection throughout the year.

The barrier to the south is difficult to discuss, because we do not yet know how far the infected region extends to the south and east of Nigeria. Plans are being made for an immunity survey of parts of French Equatorial Africa and the French Cameroons by governmental health officials and the West African Yellow Fever Commission of the Rockefeller Foundation. Arrangements have been made also for a similar study in the Belgian Congo. There the blood specimens will be collected by governmental health officials and sent to the Commission's laboratory in Lagos for examination. It is hoped that a survey can be made in Angola also. Pending the results of these investigations, we have only the published reports of outbreaks to guide us. As has been previously mentioned, yellow fever has been reported as far south as Angola. Near the southern boundary of Angola and in the northern part of South West Africa there is a region of low rainfall and sparse population which extends far into the interior. It would tend to retard the advance of yellow fever if the disease should be found in the Congo region or northern Angola.

The obvious barrier on the east is the high and mountainous lake region separating the Congo basin from East Africa. A study of the climatic factors which might inhibit the breeding of *Aedes aegypti* in this region and a survey of the prevalence of these mosquitoes in populous places and along routes of travel would give most useful information. It seems improbable that the well-watered equatorial forests of French Equatorial Africa and Belgian Congo, from which yellow fever has never been reported except near the coast, is unfavourable to the spread of yellow fever where the population is adequate. Unknown factors may exist, nevertheless, and a study of the density of *Aedes aegypti*, and the customs of the natives with regard to water storage would be valuable. The region on the boundary between French Equatorial Africa and the Anglo-Egyptian Sudan requires investigation, particularly with regard to the prevalence of the mosquito vector in relation to the density of population.

The possibility that improved methods of travel, particularly by railway trains, motor vehicles, and aircraft, might carry yellow fever through barriers heretofore effective has caused considerable concern. As yet, there has been no evidence that yellow fever has been carried by aircraft in Central or South America. Some of the recent outbreaks in Brazil and Bolivia seem to have been the result of the introduction of non-immune persons, usually troops or refugees from a drought-stricken district, into a region in which most of the people were immune and the presence of a small amount of yellow fever was unrecognized. As soon as the disease becomes actively epidemic in a community and involves many cases, the number of infective mosquitoes and of infected persons travelling during the incubation period may be assumed to rise rapidly. This increase in the carriage of virus into surrounding communities puts a severe test on their resistance to invasion. Epidemics appear in towns which were free of infection or were quietly keeping up a partial immunity of their population by occasional unrecognized infections or small outbreaks. Such it seems to me is the explanation of the extension of yellow fever in Brazil during and after the recent epidemic in Rio de Janeiro, and of the appearance of a succession of epidemics in groups of African towns. Evidently the prevention of epidemics, especially in centres of travel, and the suppression of such outbreaks, when they have been allowed to occur, are essential measures for the protection of infectible places, at a considerable distance. The infected territory cannot be expected to carry the whole burden, however, especially now that the extermination of the disease in Africa seems remote, and the vulnerable regions should protect themselves by making their key cities as nearly non-infectible as possible. In addition, it would be wise to exercise a degree of control over rapid travel from infected to non-infected territory.

That *Aedes aegypti* may survive long flights in aeroplanes has been demonstrated by Griffiths and Griffiths. They drew the conclusions that 'with conditions at airports such as would permit of many mosquitoes getting abroad, it might be expected that approximately one-fifth of the original number would be transported for a long distance—at least 1,250 miles—in one day, with repeated landings and opening of doors, hatches and windows, and refuelling, unloading, and loading taking place'. They were of the opinion that there is no obstacle to the efficient treatment of aeroplanes so as to destroy mosquitoes. The risk of carrying persons in the incubation period of yellow fever seemed to be of greater importance than the transfer of infected mosquitoes.

Protective measures against yellow fever in Africa must be based on a full knowledge of the situation if they are to be effective. The Office International d'Hygiène Publique has urged the extension of the present immunity survey to other regions of Africa. I have mentioned the plans for the Belgian Congo and French Equatorial Africa. In East Africa it would seem

advisable to confirm the supposition that the region is entirely free of infection by taking serum samples from natives in a few representative centres. Health officials in the British Crown Colonies who wish to participate in such an immunity survey can arrange for the laboratory tests through Dr. G. M. Findlay and should send the blood specimens to him at the Wellcome Research Institute in London. He will decide whether to make the tests there or send the specimens on to the Yellow Fever Laboratory in New York.

There are three other annexes by the representatives of the Gold Coast, Angola and Tanganyika Territory describing the conditions in their own particular area. The most striking thing in these statements is the apparent unanimity in regarding motor transport as more potentially dangerous than air transport in spreading yellow fever.

The report ends with a statement on another danger arising from aerial travel which has hitherto received little attention; it is given below:—

TRANSMISSION OF ANIMAL DISEASES BY AEROPLANES

By DR. P. J. DU TOIT

Director of Veterinary Services for the Union of South Africa

When rinderpest swept over South Africa in 1896-97, it was observed that the disease advanced at about the same rate as an ox-wagon. To-day the rate of progress would probably approximate more closely the speed of a motor-car or aeroplane. Vehicular transport has become an important factor in the spread of animal diseases.

One example may suffice to prove the truth of this statement. In August 1918, a dog was smuggled into England from the Continent by aeroplane and was landed at Plymouth. It developed rabies, which spread to seventeen counties, and it was only after a very energetic and costly campaign, lasting three years, that the disease was again eradicated.

South Africa is exposed to this danger in a very special degree, because all aeroplanes entering the Union of South Africa have to pass over tropical countries which harbour many dangerous diseases. Other countries, which are free of these diseases and which lie on the route followed by the aeroplanes, are, of course, exposed to the same dangers. These diseases may be conveyed in three ways: by means of live animals; by means of insect vectors; by means of products containing the infective material.

These three methods may be elucidated briefly.

(a) INTRODUCTION OF DISEASES THROUGH LIVE ANIMALS CONVEYED BY AEROPLANES

At present the danger is practically confined to domestic pets (especially dogs), although in the future the conveyance of larger domestic animals by air may become an everyday occurrence.

Some of the diseases which may be transmitted in this way are the following:

(1) *Rabies*.—This disease has already been mentioned, and measures to guard against the introduction of possible carriers are urgently needed. The long incubation period and the susceptibility of practically all animals (and man) enhance the danger of conveying rabies by air.

(2) *Foot-and-mouth disease*.—The recent, unexplained outbreak of this disease in Southern Rhodesia makes us suspect the aeroplane as a possible carrier of infection. Again, several species of animals (and also man) are susceptible to this disease. In view of the enormous financial burden which an outbreak of this disease imposes on a country, it behoves us to take every possible precaution against its introduction.

(3) *Rinderpest*.—The disease is enzootic in Central Africa, but absent from Southern Africa. Its introduction would be in the nature of a national calamity. In addition to cattle, sheep, goats, and various antelopes

are susceptible; and the transmission of the disease by means of these smaller animals is not beyond the bounds of possibility.

(4) *Lung-sickness (pleuro-pneumonia of cattle)*.—Southern Africa has been free of this disease for many years, although it is prevalent in other parts of Africa.

(5) *Sheep-pox* also is absent from Southern Africa, and its introduction would probably involve the country in very serious expense.

(6) *Hog cholera (swine fever)*.—The European (and American) form of the disease does not occur in South Africa, whereas we have another form of the disease which is also present in other parts of Africa. Recovery from either form of the disease fails to protect against infection with the other. The introduction of the European virus into Africa, or of the African virus into Europe, is therefore liable to cause very serious economic losses.

(b) INTRODUCTION OF DISEASE BY MEANS OF 'INSECT' VECTORS CARRIED BY AEROPLANES

The chief danger lies in ticks. These arthropods, which transmit some of the most important animal diseases, can easily be conveyed on the clothing or luggage (rugs) of passengers travelling by aeroplane. Since infected ticks can live without food for a year or longer, the danger of introducing disease in this way is obvious.

A few examples may be quoted to illustrate the danger.

(1) *East Coast fever (Theileria parva infection of cattle)* has been, or is being, eradicated from some African countries at enormous cost, whereas it remains enzootic in others. The introduction of infected ticks into countries free of the disease would be calamitous.

(2) *Anaplasmosis* is a very fatal disease of cattle. The ticks which transmit it are present in all parts of Africa, whereas the disease itself is absent from many countries (e.g., West Africa). One infected tick could start the disease in such countries.

(3) *Nairobi disease (gastro-enteritis) of sheep* is a virus disease transmitted by ticks which are present over the greater part of Africa. As far as is known, the disease is confined to a comparatively small area in Kenya. But there is nothing to prevent the disease getting a foothold in other countries if infected ticks were introduced.

(c) INTRODUCTION OF DISEASES BY MEANS OF PRODUCTS CONTAINING INFECTIVE MATERIAL

The outbreak of foot-and-mouth disease in the United States of America in 1908 was traced to the introduction of contaminated vaccine lymph. In another instance, hog cholera serum was responsible for the spread of foot-and-mouth disease. The importation of vaccines and sera by air or otherwise should be carefully controlled.

Other objects capable of carrying infection are skins, horns or other parts of animals which air passengers may collect during their travels. The danger of introducing diseases like foot-and-mouth disease in this way is very great.

RECOMMENDATION

Consideration should be given to the desirability of national regulations and international agreements to prevent, as far as possible, the transmission of animal diseases by aeroplanes.

Although this note of Dr. Du Toit applies particularly to the southern half of the African continent many of the points touched upon are of importance to other countries.

ABSTRACT OF REPORT OF A MEETING OF THE ROSS INSTITUTE INDUSTRIAL ADVISORY COMMITTEE HELD ON WEDNESDAY, 1ST FEBRUARY, 1933

SIR MALCOLM WATSON spoke in more general terms on conditions in countries other than India where the Ross Institute is operating.

Dr. Ramsay drew attention to the danger of accepting the behaviour of certain mosquitoes in the laboratory as an indication of what the same species will do in nature quoting examples from his own experience. He then gave an account of the first scheme tried in Assam in the use of atabrin and plasmoquine in prophylaxis of malaria quoting from a letter written by the superintending medical officer who was in charge of the garden where this experiment was carried out.

'After writing to you on the 15th instant, I received a full report from my assistant medical officer about the results of the Blanket treatment with atabrin and plasmoquine, and went up myself to investigate.

'After the fourth day of treatment, three people complained of headache, vomiting and purging, and the passing of red coloured urine, and were kept under observation.

'On the fifth day after the morning dose 11 people were kept under observation with the same symptoms, and three had slight jaundice. Eight of these had a heavy cloud of albumin in the urine.

'The day after the completion of the course, which was Sunday, nine more people were admitted; two of these were suffering from all the symptoms of black-water fever, the urine being of a very dark porter colour, with a slight reddish tinge and the other quite black. Both these, on microscopical examination, showed many red blood corpuscles, renal epithelium and much cell debris. The urine of the other cases varied from an orange colour tinged with pink to light red, dark red to almost black.

'On Monday about 60 people applied for sick leave—the chief complaint being gastric pain. Twenty of these were considered to be malingering and were sent to work, which left matters as follows:—

'Out of a working force of 114 adults and 20 children—134, there were:

Indoor patients	22
Out-patients	40
Attendants	10
				—
				72
				—

'All the cases cleared up rapidly after purgation, except the two apparent B. W. F. cases, and when I had a muster on the Friday following the treatment they seemed to be all right and no complaints.

'The manager had stopped the beginning of plasmoquine until I had investigated the matter, and the first dose of 3×0.01 was given on Friday—six days after the end of the Blanket treatment'.

The dosage is not indicated in the above communication but it is presumably the same as that employed by Dr. Fraser given in his report below. In view of the above alarming report he gave his own investigation the *closest personal supervision*.

The garden on which the experiment was done was seriously affected by malaria in 1921, when it had been black-listed by the government. The spleen rate at that time was about 100 per cent. The mosquitoes causing the malaria came from ravines which intersected the garden in every direction. The ravines were gradually being rendered harmless by permitting the growth of bamboo and other dense forms of vegetation over the streams in these ravines. Oil and Paris-green were still used in places where the shade was not yet effective, but it was hoped in time to create such a growth over all breeding places that malaria would be permanently controlled at no cost by this method. The spleen rate at the end of December 1931 had been reduced to 43 per cent, and this was largely due, he thought, to having let the dense jungle grow, instead of clearing it as had previously been done. The garden had a population of roughly 500 living in compact lines. The garden was fairly isolated, being situated rather more than half a mile from the nearest habitation.

The spleen rate of children on 13th September, 1932, was 56 per cent (middle of transmission season). The total parasite rate immediately prior to treatment, 52 per cent. The gametocyte rate prior to treatment was 12 per cent.

Commencing from 19th September, atabrin was given for five days in doses of one tablet in the morning and two tablets in the evening (each tablet 0.1 gramme), and proportionately for children.

The slides of the gametocyte carriers only were taken after atabrin (but before plasmoquine), and showed a disappearance of benign tertian, but a persistence of quartan and malignant gametocytes, particularly the latter.

A treatment of plasmoquine was then given for five days from 25th September. The parasite rate taken shortly after the atabrin-plasmoquine treatment was 11.5 per cent. There was only one gametocyte found.

Subsequent anti-gametocyte treatment beginning 6th October was given to the whole population on two consecutive days a week for eight weeks, with a view to preventing the spread of infection, and all cases of active malaria occurring after the initial treatment were re-treated until free from parasites.

On 27th December, 1932, three months after the beginning of treatment, the spleen rate in children was 26 per cent. Special points as regards treatment were:—

Plasmoquine was given after food during the treatment, and in doses of 0.01 gramme twice daily for adults.

On the fifth day of plasmoquine treatment, 0.01 gramme and 0.02 gramme were given morning and evening respectively. Proportionate doses were given to children. In the subsequent anti-gametocyte weekly mass treatment, plasmoquine was given irrespective of meal-times. Weakly or anemic cases were treated in hospital. *There were no complications, either with atabrin or plasmoquine.* In fact, the coolies were very enthusiastic about the treatment.

The immediate results of this experiment have been very satisfactory. Although, however, the garden lent itself admirably to the purposes of the experiment, yet it was found that the movement to and from the garden could not be controlled, which is essential if the population is to be kept free from infection; there was also difficulty in getting all people who developed a temperature subsequently to present themselves for blood examination. From the parasite rates shown there was an immediate failure rate of over 21 per cent. In addition, there were 50 cases of malaria from 19th September to 31st December; many of these, no doubt, were relapses, but many, especially the later cases, were in the opinion of the investigator reinfections. It appeared, too, that many cases were refractory to atabrin, even when the dose was increased by one-half for six days.

The position now is, however, that malaria has been reduced to a very low level amongst the human population and also in the mosquito population. Whether it will continue at this low level by the treatment of individual infections cannot be said. There will be a new survey at the beginning of next transmission season, and it will be decided whether the treatment be repeated or whether the results of that just given should continue to be observed. The treatment of this population cost nearly Rs. 2,000, which it was agreed should be paid partly by the Ross Institute, and partly by Messrs. Bayer. It cost over Rs. 3 a head, but the makers hope to reduce this to about Re. 1, partly by getting the government to remove the 25 per cent import duty on the drug, as is done in the case of quinine.

It will be seen from this experiment that it is still too early to draw any final conclusion as to the possibility of eliminating malaria or keeping it at a permanently low level by means of atabrin and plasmoquine.

Dr. Manson also described some experiments with these drugs but his work is not sufficiently advanced to allow him to express an opinion.

Both Drs. Fraser and Manson after giving anti-dysentery bacteriophage an extensive trial are very definitely of the opinion that it is valueless in treatment.

Correspondence

ASSOCIATION OF MEDICAL WOMEN IN INDIA

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—The undernoted resolution was passed at a meeting of the Northern Division of the Association of Medical Women in India, and later was adopted by the Council of the Association.

'In the opinion of this meeting the time has come for reconsidering the allotment of Medical Women for work in India. The efficiency of the work would be enormously increased if there were groups of medical women working together, each being a specialist in her own subject, e.g., surgery, medicine, gynaecology and obstetrics, and pathology. In this way there would be centres of highly organized work in large cities where (a) surrounding dispensaries could refer their more serious cases for treatment; and (b) post-graduate work could also be carried on. These centres might employ honorary workers in addition to the paid staff of specialists'. The reasons given in the discussions which led to the resolution were as follows:—

Medical work in most hospitals in India at the present time is not up to the same standard as in Europe. The reason for this is partly that medical officers have no time to carry on careful and detailed clinical and pathological examinations, and partly that medicine has now become so highly specialized that one or two doctors cannot hope to be experts in all departments. Under the present system where one medical woman is in charge of a small hospital with one qualified assistant, or even where two medical women are in charge of a larger hospital with two or more assistants, it is impossible to keep pace with the many new methods both for diagnosis and treatment. We lose many opportunities of successful treatment, and each time we lose the confidence of a patient. In some towns there are two or three hospitals, each of which may be poorly equipped and all of which are poorly staffed according to modern ideas. These hospitals have done excellent pioneer work and have gained the confidence of the public, but no one knows better than the doctors in charge that very much better work might be done, and very much greater success attained, if the doctor had more leisure for thought and study, and especially if they were able to concentrate on one department of the work and refer other cases to colleagues specially trained to receive them. The need being so clear we feel the time has come to put the matter forward, and to try for a complete reorganization of medical relief in India, or at least in the smaller towns and districts, for the system we are advocating exists to some extent in the larger towns and teaching institutions.

No doubt there would be difficulty at the present time in getting additional expenditure met, but would it not be possible for different charitable organizations to close down neighbouring institutions, and pool all their resources on one institution organized in the manner indicated above. A chain of dispensaries through the surrounding district would keep in touch with the hospital. In the end more good would be done even if a smaller number of in-patients were treated.

Although our discussion related chiefly to women's hospitals, there is no doubt that similar reorganization is equally needed for men's hospitals.

Yours, etc.,
RUTH YOUNG,
President.

VACCINATION AGAINST SMALLPOX

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—On p. 242 of your issue of April 1933 appears a letter regarding 'Vaccination against Smallpox', with a note in reply thereto by Lieutenant-Colonel A. D. Stewart, I.M.S., to which I should like to add one or two comments.

Firstly, is it not possible that, when a tube of lymph is assessed as sufficient for 4 persons, the manufacturers have gauged the amount necessary for use by the clumsiest vaccinator with the worst technique?

Secondly, I would make a plea in favour of more attention being paid to the finer points of vaccination technique at schools of instruction. With ample opportunity for noting methods and results of vaccinations done in different parts of India, we have found them to vary in appearance from pin-pricks to attempted amputations, and we have also been struck by the diverse methods employed. The object of vaccination is to split the epidermis and to inoculate the virus no deeper than the region of the stratum granulosum and stratum Malpighii.

In some parts of India vaccinators scarify the arm, and then when it is nice and bloody they mop on the lymph through the oozing mess; the result, apart from possible sepsis, is that nothing happens, for the lymph is either washed away in the gory stream or so diluted as to be ineffectual. For this reason I object to the circular drill seemingly approved in the last paragraph of Colonel Stewart's note.

In highly skilled hands the drill may possibly be successful, but I submit that it can never be as good as a cutting edge or point. For manufacturing reasons the edge of the drill must be relatively broad so that on circular scarification a ditch is produced rather than a split, and, whereas the latter, on swelling, closes over the inoculated virus, the former in comparison is flushed by oozing serum from the bottom and sides, and the virus stands relatively less chance of establishing itself.

The truth of this assertion has frequently been suggested by the success of lancet-scarification after drill-vaccination has failed.

Dr. A. E. Cope, of Westminster Hospital, used to teach that a good vaccination should after a minute or two show only the minutest blood speckling along the lines of scarification and that no drop of blood should flow.

A few years ago an overseas port was infected with smallpox, and vaccination with drills produced a regrettable number of failures. The drills were scrapped, lancets imported, and demonstrations in technique given to the specially enrolled vaccination staff who were taught to put three small beads of lymph, each about the size of millet seed, spaced vertically upon the cleansed skin, and to vaccinate *through* these with only 3 or 4 vertical parallel scarifications each about $\frac{1}{4}$ inch long. The result was a most satisfactory crop of successes, practically no sepsis, phenomenal popularity of vaccination inasmuch that some who applied for vaccination were found to have been done already on the other arm or leg (presumably vaccination certificates were proving to be of marketable value), and cessation of the epidemic, if I remember aright, within about 6 weeks.

It is true that, in a population of about 58,000, about 78,000 vaccinations were performed which suggested that both the population and the vaccinators meant to do the thing properly, but I still maintain that it was the latter's technique to which the success was due; it was found that, with a tube estimated by the manufacturers as sufficient for 10 persons, between 30 to 42 persons could be satisfactorily vaccinated, according to the lightness of touch of the vaccinators of whom, strangely enough, a Somali girl proved to be the best.

Yours, etc.,
C. L. B.

BOMBAY,
26th April, 1933.

THE OCCURRENCE OF HÆMOGLOBINURIA DURING TREATMENT OF MALARIAL FEVER WITH ATEBRIN AND PLASMOQUINE

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I was interested to read in the last (March) issue of the *Indian Medical Gazette* the article of Drs. Banerjee and Brahminchari on the occurrence of hæmoglobinuria during treatment of malarial fever with atebrian and plasmoquine, as a similar case passed through my hands in November last.

As I am beginning to feel that there is some connection between the hæmoglobinuria and plasmoquine, I am narrating below the case which was attended by me.

A young college student started getting fever in the beginning of October 1932. He was treated with quinine and the fever left him in five or six days. In the last week of October 1932 again he started getting fever; he was similarly treated with quinine, but to no effect. He was therefore put on plasmoquine compound tablets, one pill thrice daily. Three days after the administration of plasmoquine the patient passed a large amount of hæmoglobin in his urine, his skin became dark and the eyes jaundiced. He was diagnosed to be a case of blackwater fever. Plasmoquine was therefore stopped. He was treated with alkalies and blood transfusion, followed by intravenous glucose and citrate, without improvement. The patient ultimately died on the third day after the appearance of hæmoglobinuria.

Fortunately, some pills out of the phial of plasmoquine were left over; these I passed on to the Professor of Pharmacology in the Medical College here. He experimented with them on dogs, but could not detect any toxicity in the drug.

During the last autumn another two cases of blackwater fever occurred here and in each one of them the hæmoglobinuria appeared after the administration of plasmoquine. Suspicion has therefore been aroused in one's mind, does plasmoquine play any part in the causation of hæmoglobinuria? Though on the other hand hundreds of cases of malarial fever have been treated with plasmoquine without any untoward effects.

Yours, etc.,
GOPAL SINGH CHAWLA,
CAPTAIN, M.D., B.S.

LAHORE,
23rd March, 1933.

ANTI-RABIC TREATMENT

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Can anti-rabic treatment be carried out in remote villages without sending the patients to anti-rabic centres?

A search through literature tells us that nowadays anti-rabic vaccine can be sent out in ampoules to different parts of the country, thus doing away with the necessity of maintaining centralized anti-rabic institutes.

Is the potency of the vaccine affected in any way during transit and storage at the ordinary room temperature?

How long is its potency maintained when it has left the laboratory?

Now provided its potency is maintained, from what sources may we obtain a supply of the vaccine at a minimum cost?

As, at present, it is not available from the ordinary druggist's shop, so we must look to some anti-rabic centre such as Shillong or Calcutta for its supply.

Yours, etc.,
A. K. GHOSE, L.M.F., L.T.M.,
Medical Officer.

AMBARI TEA ESTATE,
CARRON P. O.,
JALPAIGURI.

[Note.—We submitted Dr. Ghose's letter to Dr. M. J. Nicholas who is in charge of the Pasteur Institute at the Calcutta School of Tropical Medicine; he kindly supplied the following information:—

'Anti-rabic treatment cannot be carried out in remote villages because no facilities exist in these places for the administration or storage of the vaccine. Most provinces have now established treatment centres at District Headquarters hospitals where treatment is available for patients from the surrounding villages. Arrangements for such a scheme are in progress in Bengal at present.

The potency of the vaccine is not affected during transit, but it should be stored in a cool place and not at ordinary room temperature.

When stored in the cool and screened from light the vaccine retains its immunity for a period of four months from date of manufacture.

The source of supply is from the Pasteur Institute of the Province.

The reason why anti-rabic vaccine is not sent out from Calcutta at present is because no facilities exist for the bottling of the vaccine in ampoules, and the only safe method of sending out vaccine is in ampoules'.—Editor, I. M. G.]

A LEECH IN THE NASAL CAVITY AND ITS REMOVAL

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—On page 212 of your issue of April 1933 appears a note entitled 'A Leech in the Nasal Cavity and Its Removal', which prompts me to draw attention to a method of dealing with the situation which may not be generally known, but upon which I stumbled by accident in Bakloh some years ago. An Officer of the local regiment brought to me his spaniel which had been afflicted for some days with a leech in the nose. We tried the water treatment, but the leech retracted up again when touched by the forceps, and nasal lavage with saline appeared to disturb the dog more than the leech! All efforts at holding the animal still having proved ineffectual, I gave him a few whiffs of chloroform, and long before the dog showed signs of going under, the leech lay limply in the animal's nostril and was easily withdrawn.

I recommended this method to a friend in Burma some years later, and it was tried with equal success. If therefore leeches are so susceptible to chloroform, perhaps administration through a Junker or similar apparatus, up the affected nostril in human beings would be equally successful?

Yours, etc.,
C. L. B.

BOMBAY,
25th April, 1933.

ANTIPHLOGISTINE SUBSTITUTES

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Regarding the note on Antiphlogistine substitutes in your paper last month (March 1933), I beg to record my experiences.

I have an ample opportunity of testing the efficacy of various antiphlogistic plasters in various diseases, on the students in the Gurukula Kangri, an educational institution. More than 600 students reside in the boarding house.

All the Indian preparations that I tried are lacking in the power of retaining heat for more than one or two hours; on the other hand the American preparation, Antiphlogistine, retained its heat for about 6 or 7 hours. My patients suffering from acute pharyngitis and tonsillitis always complained of the Indian preparations feeling very cold in the morning after applications at night. This is also my own experience.

The second point of difference is that the Indian preparations are either too hard to stick to the lint and

have no hygroscopic power, or they are not properly dehydrated. A chemist friend of mine informs me that the hygroscopic quality does not depend merely on putting glycerine in the preparations, but that they require dehydration by proper chemical methods. A patient of mine told me that he softened the hardened mass of an Indian preparation by putting in some water; this is still worse as the water evaporates and leaves the plaster as hard flat pieces on the skin which fall down from underneath the piece of lint.

The only drawback in the use of the American preparation is its price which is about two and a half times the price of the same bulk of the Indian

preparations. If the Indian manufacturers can improve their stuff, and satisfy both the physician and the patient, there is no doubt that there would be a big demand for their products.

Yours, etc.,

RADHA KRISHNA GROVER, B.Sc., M.B., B.S.,
Chief Medical Officer.

GURUKULA RESIDENTIAL
UNIVERSITY,
GURUKULA KANGRI (HARDWAR).
30th March, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL H. HINGSTON having vacated the post of Surgeon to His Excellency the Governor of Bengal on completion of the term of his appointment, His Excellency has been pleased to make the following appointments:—

(1) Lieutenant-Colonel J. D. Sandes, Professor of Medicine, Medical College, Calcutta, to be Honorary Physician to His Excellency.

(2) Major S. A. McSwiney to be Honorary Surgeon to His Excellency while holding the appointment of Civil Surgeon, Darjeeling.

Lieutenant-Colonel N. C. Kapur, Civil Surgeon, Chittagong, is appointed to act as Superintendent of the Campbell Medical School and Hospital, with effect from the date on which he takes over charge of his duties.

Lieutenant-Colonel P. F. Gow, D.S.O., Professor of Midwifery, Medical College, Calcutta, is appointed to act as Principal of the institution in addition to his own duties, *vice* Lieutenant-Colonel T. C. Boyd.

Lieutenant-Colonel J. C. De, Professor of Clinical Medicine, Medical College, and Second Physician, Medical College Hospitals, Calcutta, is appointed to act as Superintendent of the Medical College Hospitals, Calcutta, in addition to his own duties, *vice* Lieutenant-Colonel T. C. Boyd.

Lieutenant-Colonel J. Morison, C.I.E., Director, Pasteur Institute and Medical Research Institute, Shillong, is appointed to officiate as Inspector-General of Civil Hospitals and Inspector-General of Prisons, Assam, *vice* Colonel J. P. Cameron, C.S.I., C.I.E., who has been granted leave.

Lieutenant-Colonel H. C. Buckley, Civil Surgeon, Lucknow, is appointed to officiate as Inspector-General of Civil Hospitals, United Provinces, with effect from the afternoon of the 25th March, 1933, and until further orders.

Lieutenant-Colonel C. I. Brierley, C.I.E., Chief Medical Officer, North-West Frontier Province, is appointed Inspector-General of Civil Hospitals, North-West Frontier Province, with effect from the 17th February, 1933.

Lieutenant-Colonel M. A. Nicholson, an Agency Surgeon, on return from leave is posted as Chief Medical Officer in Central India and Residency Surgeon, Indore, with effect from the forenoon of the 23rd March, 1933.

Lieutenant-Colonel R. F. D. MacGregor, M.C., an Agency Surgeon, is posted as Residency Surgeon, Hyderabad, with effect from the afternoon of the 30th March, 1933.

Lieutenant-Colonel F. Stevenson, an Agency Surgeon, is posted as Residency Surgeon and Chief Medical

Officer in Baluchistan, with effect from the afternoon of the 21st February, 1933.

Major W. J. Webster, M.C., an officer of the Medical Research Department, is appointed as a Supernumerary Officer at the King Institute, Guindy, Madras, with effect from the 4th March, 1933.

Major R. L. Vance, an Agency Surgeon, is posted as Chief Medical Officer in the Western India States Agency and Residency Surgeon, Rajkot, with effect from the forenoon of the 30th March, 1933.

Major R. S. Aspinall is appointed to be Civil Surgeon, Simla East, with effect from the 1st April, 1933.

Major S. D. S. Greval, an officer of the Medical Research Department, is appointed as a Supernumerary Officer at the Haffkine Institute, Bombay, with effect from the 1st April, 1933, until further orders.

Major B. G. Mallia is appointed as Civil Surgeon, Chittagong, *vice* Lieutenant-Colonel N. C. Kapur transferred.

The services of Major J. Chandra are placed permanently at the disposal of the Government of Bihar and Orissa for employment in the Bihar and Orissa Jail Department.

The services of Captain G. M. Irvine are placed temporarily at the disposal of the Government of Burma, with effect from the date on which he assumes charge of his duties.

The services of Captain B. S. Nat are placed permanently at the disposal of the Punjab Government, with effect from the 10th November, 1932.

To be Captains

Captain (local Major) F. M. Collins, from R. A. M. C. Dated 24th January, 1933, with seniority 1st September, 1929.

Captain C. V. D. Rose, from R. A. M. C., 14th February, 1933, with seniority 25th October, 1922.

To be Captains (on probn.)

P. V. Karamchandani. Dated 13th January, 1933, with seniority 26th February, 1926.

R. K. Misra. Dated 11th January, 1933, with seniority 2nd April, 1926.

K. R. Sahgal. Dated 22nd December, 1932, with seniority 26th September, 1926.

To be Lieutenants

B. A. Porritt, 20th February, 1933, with seniority 26th July, 1930.

M. S. Purvis, 20th February, 1933, with seniority 20th February, 1932.

F. W. Whiteman, 1st February, 1933, and remains seconded.

M. E. Kirwan, 20th February, 1933.

To be Lieutenant (on prob.)

W. S. Morgan, 13th February, 1933.

LEAVE

Colonel J. P. Cameron, C.S.I., C.I.E., Inspector-General of Civil Hospitals and Inspector-General of Prisons,

Assam, is granted combined leave for 5 months, with effect from the 20th May, 1933, or subsequent date from which he may avail himself of it.

Colonel R. McCarrison, C.I.E., K.H.P., an officer of the Medical Research Department on foreign service under the Indian Research Fund Association, is granted combined leave, with effect from the 28th April, 1933, for 6 months and 8 days. His services will be placed at the disposal of the Director-General, Indian Medical Service, from the date on which he proceeds on leave.

Brevet-Colonel G. D. Franklin, C.I.E., O.B.E., K.H.S., an Agency Surgeon, is granted leave, preparatory to retirement, for 6 months and 15 days on average pay combined with leave on half average pay for 9 months and 13 days, with effect from the afternoon of the 30th March, 1933.

Lieutenant-Colonel J. B. Hance, O.B.E., an Agency Surgeon, is granted leave on average pay for 2 months combined with leave on half average pay for 5 months, with effect from the afternoon of the 26th March, 1933.

Lieutenant-Colonel R. B. Seymour Sewell, Director, Zoological Survey of India, is granted leave out of India on average pay for 1 month and 3 days combined with leave on half average pay for 21 months and 8 days, preparatory to retirement, with effect from the 22nd April, 1933.

Lieutenant-Colonel V. N. Whitmore, O.B.E., Civil Surgeon, Simla (West), is granted leave on average pay for three months and 20 days, with effect from the afternoon of the 30th November, 1932, to the 20th March, 1933, inclusive.

Previous notification granting him leave on average pay for 4 months is hereby cancelled.

The notification of February 1933, granting leave to Colonel H. R. Nutt, Inspector-General of Civil Hospitals, United Provinces, is cancelled.

Major J. P. Canteenwalla, Officer in charge, Medical Store Depot, Calcutta, is granted privilege leave from the 18th April to 27th May, 1933.

Major S. D. S. Greval, an officer of the Medical Research Department, is granted leave on average pay for 4 months, with effect from the 15th April, 1933, or the date from which he may avail himself of it.

In supersession of previous notification of the 5th April, 1933, Captain (local Major) F. M. Collins, Surgeon to His Excellency the Viceroy, is granted leave for 3 months and 11 days, with effect from the 7th April, 1933. On the expiry of this leave his services will be placed at the disposal of the Army Department.

PROMOTIONS

Lieutenant-Colonel to be Colonel

W. T. McCowen. Dated 12th February, 1933, with seniority 30th July, 1927.

Lieutenant (on prob.) to be Captain (provl.) (on prob.)
Dev Datt. Dated 10th October, 1932.

RETIREMENTS

Lieut.-Col. G. M. Millar, O.B.E., 24th February, 1933.
Colonel P. L. O'Neill, C.I.E., 28th February, 1933.

Notes

PROFESSOR PICCARD'S EXPERIMENT

Our readers will remember that their balloon ascent to the stratosphere enabled Messrs. Piccard and Kipfer to measure the electrical conductivity of the air and the cosmic radiation intensity in the high atmospheric layers, up to the unbelievable altitude of 16,000 metres.

The next ascent to be effected by Professor Piccard has as aim the completion of these measurements, which had been limited on the previous occasion owing to the very rapid ascension and the dismounting of the apparatus before the descent. These new data will undoubtedly lead to the determination of the exact value of the cosmic radiations as a function of the

altitude, and perhaps even to an understanding of the precise nature of these radiations.

Professor Piccard has taken the precaution to have the principal weldings of the aluminium cabin examined by means of x-rays. The photograph here shown was taken recently in Professor Piccard's laboratory at the Brussels' University. The x-ray apparatus, chosen by Professor



Piccard, is a 'Metalix' portable which can penetrate up to 50 mm. of aluminium with an exposure of a few seconds. The type of apparatus for 180,000 volts which can penetrate 100 mm. of iron, especially designed for metallography, was not deemed necessary. The numerous radiographs of the weldings which surround the two doors of the cabin and the eight vertical supporting bars could be taken with greater facility than would have been the case if a larger instrument had been used, as the apparatus was of the portable type and integrally protected against the high tension and the secondary irradiation emitted by the tube.

WATSON'S MICROSCOPE RECORD

THE last number of Watson's *Microscope Record* has maintained the standard set by its predecessors in providing matter of considerable interest to all microscopists. In this number, no. 28, the Editor has concluded his very practical note on dark-ground illumination. There are a number of diagrams which illustrate the earlier developments of this method, and the note is concluded with a list of instructions for obtaining good dark-ground illumination; these are quite worth copying and distributing to students or laboratory assistants. Other articles are on water-moulds, on the structure of diatoms, and on the fresh-water polyzoa.

One of the microscopes that is described in some detail is what we usually call a 'dissecting microscope', but the use of such an instrument is much beyond the simple dissection of mosquitoes. In many commercial enterprises an instrument of this nature is in daily use. This particular instrument achieves a very high degree of perfection and is in consequence not very cheap, but it appears to be good value for the money; it is priced at £17-10. An extract from the description may be of interest to our readers:—

In textile factories, paper mills, chemical works and in the laboratories of dozens of industries microscopes

of the lowest power are necessary implements. In the prosecution of biological studies related to agriculture, animal husbandry and fisheries a low-power microscope is a daily assistant. In tropical medicine, and especially in connection with work on insect hosts, the use of such a microscope is of vital importance and ministers to the safety of millions of human beings.

This being so, the low-power microscope being so necessary, it is not unreasonable to make it as optically perfect and as practically useful as possible. How is this to be done?

First, it must be a binocular, not only to give comfort to the eyes of the user, but also to provide stereoscopic vision in which objects appear in proper relief.

Also the low-power microscope should provide an erect image so that manipulation or dissection of the object is effected without confusion of movement.

As the erecting binocular low-power microscope is so useful it is an advantage to be able to apply it to a variety of objects. It should be applicable to a large specimen or a small one, therefore it should have a stand with considerable extension and with a clamp to fix it rigidly at the right height. Finally, it may have a change of power effected rapidly, as, for instance, by the revolution of the nosepiece.

All these desirable features will be found incorporated in Watson's low-power binocular microscope; it also possesses a special departure from the Greenough type of instrument in the much more rigid single body with parallel eye-tubes adjustable for width of eyes. This new type of binocular is much more easily adjusted by the observer and is offered as a more practical instrument than earlier types for work on a great variety of objects.

There are, of course, thousands of technologists who ought to have a low-power binocular microscope on their laboratory benches, and doubtless hundreds of these are contemplating the purchase of such an instrument in the near future. May we suggest that they consider the advantages possessed by this instrument.

EPHEDRINE B. D. H.

In Asthma: The vaso-constriction produced in the mucosa by the administration of this drug causes prompt alleviation of the characteristic distressing symptoms (*B. M. J.*, 1930, 1, 873). In fact, results of recent investigation indicate that ephedrine is highly beneficial in the prophylaxis of asthma (*B. M. J.*, 1931, 1, 166) as well as in the treatment of the condition. Moreover, the psychological effect on the patient of the ready availability of a weapon which is known to reduce the severity of the attacks is a matter of no little importance. The effect of a single dose lasts from six to eight hours, so that one dose at bed-time ensures a comfortable night, also a dose during the day enables the patient to undertake prolonged physical effort without undue distress.

In Hay Fever: The unpleasant nasal congestion associated with hay fever, rhinitis, coryza and allied disorders may be subdued almost immediately by the administration of Ephedrine B. D. H. in one or other of its forms as may be suitable to the individual need of the patient. Ephedrine Inhalant B. D. H. (or the Inhalant Compound) being particularly active in reducing the sensitiveness of the mucous membrane.

In Whooping Cough: The benefits resulting from the administration of preparations of ephedrine in whooping cough, especially when complicated with asthma, with asthmatic bronchitis, or with bronchiectasis, have been reported upon; the results of the wide use of Ephedrine B. D. H. Elixir in ordinary clinical practice have confirmed these experimental findings.

Modes of use: Ephedrine B. D. H. is put up in a very large number of convenient forms, i.e., in tablet form for oral and for hypodermic administration, as an elixir, as an aqueous solution in ampoule form, as an inhalant, as a throat spray, and as a nasal jelly.

VITAMINS AND THE MOUNT EVEREST EXPEDITION

THE explorer of to-day realizes the tremendous importance of paying strict attention to the details of his food supply and he looks to it particularly that his provisions are adequate with regard to the essential vitamins.

The members of the Mount Everest Expedition have taken with them Marmite—the yeast extract that is known to be especially rich in vitamin B; they have taken also lemon juice and halibut oil, as sources of vitamin C and vitamins A and D, respectively.

It is obvious that good health, which sufficiency of vitamins ensures, is a vital necessity to members of any expedition if the party is to reach its goal—indeed good health is a vital necessity to every individual whether or not his particular goal be the summit of Mount Everest.

Lack of vitamin B is associated with beri-beri, pellagra, anaemia, skin complaints, constipation, digestive troubles and with many other ills. It is the opinion of many doctors that the majority of people do not ordinarily have anything like enough vitamin B unless they acquire the habit of taking some substance rich in it, such as Marmite. Marmite is taken by the Everest party as a safeguard against these ills—and incidentally it is a pleasant article of food.

Deficiency of vitamin C is responsible for scurvy, a disease that is prevalent among sailors and explorers who do not take with them enough fresh fruit and vegetables.

Vitamin A has been called the anti-infective vitamin, because it appears to play an important part in the prevention of infectious diseases.

Vitamin D is the factor that prevents and cures rickets and other diseases of the bones.

Halibut oil contains both vitamins A and D.

Thus by taking Marmite, lemon juice and halibut oil the Mount Everest party is ensuring against illnesses due to deficiency of vitamins B, C, A and D.

COW AND GATE PRODUCTS

At the All-India Sanitary and Scientific Exhibition held at Madras at the opening of the year, a Gold Medal and a Certificate of Merit were awarded to Cow and Gate, Ltd., of Guildford, England, for their well-known milk foods as exhibited by their agents, Carr and Co., Ltd. The awards were presented by Major-General C. A. Sprawson, C.I.E., V.H.S., I.M.S.

The Exhibition was visited by the Governor of Madras, Sir George Stanley, and over 2,000 medical men from all parts of India called at the Cow and Gate stall.

The awards are undoubtedly a tribute to the care and skill with which the Cow and Gate firm are catering for the special requirements of the Indian market and the increasing demand shows that their efforts to provide their nourishing foods in fresh, safe and perfect condition are appreciated by the public in general.

The importance of pure milk in India both for infants and adults cannot be over-estimated and it is a matter of general regret that actual necessities, such as these foods, should have recently been subject to an increase in the already high customs duties which are imposed upon them.

METALIX 'SENIOR' OUTFIT FOR DEEP THERAPY

We would draw your attention to a phenomenon which might give rise to difficulties when using Metalix shockproof tubes which are equipped with grids on the above-mentioned outfit. Owing to the current characteristics of such tubes the current consumption of the outfit is slightly higher than that of outfits equipped with normal Metalix shockproof tubes. It may happen that the overload relay switches off the outfit after some time. To remedy matters, the overload relay, which

has a high sensitivity, must be made less sensitive by adjusting the lever at the lower end.

It should be borne in mind that in all cases where the overload relay switches off the apparatus, the needle of the milliammeter drops to zero, the cooling pump stops and then the Neon lamp lights up.

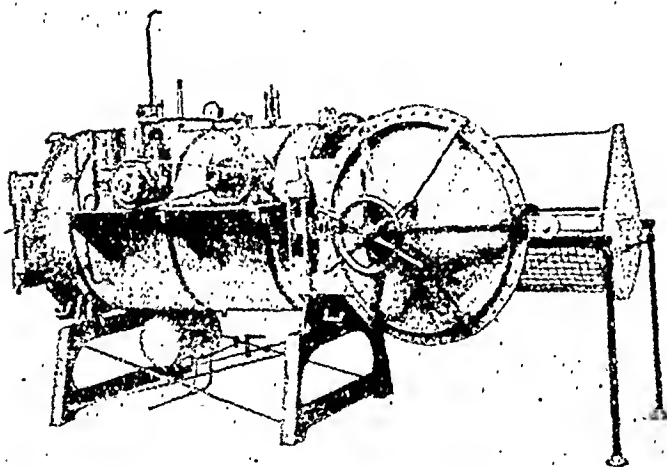
When the safety device of the cooling pump is responsible for the switching off of the apparatus, the red lamp lights up first, then the needle of the milliammeter drops to zero and the cooling pump is stopped.

VACUUM-FORMALIN DISINFECTION

RECENTLY, a disinfectant manufacturing company, in order to enlarge their sphere of activities, co-operated with a well-known bacteriologist and after eighteen months of continuous experimentation, during which time a complete disinfectant and a staff for working it were placed at the disposal of the scientist, a large amount of useful data has been obtained.

The data already obtained by scientists was investigated and it was realized that there was scope for further investigation. These further fields were explored, and after much work including extensive tests and careful recording of results not only have useful data been obtained but a great advance in disinfectant design has been achieved.

It was proved that the correct application of heat and gas will effect as satisfactory sterilization as steam, which has hitherto held the field in this type of disinfectant.



Penetration was found to be the great essential for disinfection in this heat-and-gas treatment, just as it is necessary in steam disinfection.

The ingeniously-designed disinfectant, which we show here, has an apparatus connected to the side which, by means of an electrically-driven pump, creates a vacuum inside the chamber.

The necessary heat is obtained by means of steam pipes running longitudinally, the temperature being controlled from outside at will. The heat kills all insects and complete sterilization of the contents is then brought about by the introduction of formaldehyde gas, which, owing to the vacuum, will effectively penetrate all the articles in the disinfectant.

The more complete machine manufactured by the firm is a combined disinfectant which is constructed with the steam process for the use in disinfecting such things as mattresses and heavy clothing, and the new gas system to deal with the lighter articles, such as coloured silks and leather goods, boots, etc. Thus all articles may now be effectively disinfected with the 'Velox' Combined High Pressure Steam and Vacuum Gas

Disinfectant. We believe a more comprehensive and complete machine is unobtainable at the present elsewhere.

The same firm has also devised the 'Velox' Sputum Mug and Flask Sterilizer. Again a great advance has been effected as in this new device each individual mug or flask is washed inside and outside, and after washing a pressure of 15 pounds per square inch of steam is obtained. Owing to the manner in which the articles are washed the sputum is broken up during the washing, and then sterilized.

IODISED MOOGROL (B. W. & CO.)

We have tested this preparation as to its painlessness when given by the intradermal method, comparing it with the standard hydriocarpus esters preparation containing 4 per cent crocote, as used in the leprosy department of the Calcutta School of Tropical Medicine. The two preparations were found to be of equally low irritant value. Iodised Moogrol is, therefore, suitable for injection in leprosy by both the intradermal and the intramuscular routes. As to the therapeutic value of this preparation, this could only be judged after using it in a large number of patients for a number of months or years.

As the preparation is issued by Burroughs Wellcome and Company we have no hesitation in recommending it for a thorough trial in the treatment of leprosy.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

Communications on Editorial Matters, Articles, Letters and Books for Review should be addressed to THE EDITOR, *The Indian Medical Gazette*, c/o The Calcutta School of Tropical Medicine, Central Avenue, Calcutta.

Communications for the Publishers relating to Subscriptions and Advertisements should be addressed to THE PUBLISHERS, *The Indian Medical Gazette*, P. O. Box No. 54, Calcutta.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

A CASE OF DERMOGRAPHIA WITH A SHORT NOTE ON THE ÆTIOLOGY OF THE CONDITION

By HUGH W. ACTON, C.I.E.

LIEUTENANT-COLONEL, I.M.S.

Director, School of Tropical Medicine and Hygiene
and

DHARMENDRA, M.B., B.S.

Assistant Research Worker, School of Tropical Medicine and Hygiene

Description.—In certain people the skin is hyper-sensitive to mechanical stimuli, such as stroking, scratching, or rubbing. Normally when the skin is firmly stroked with a blunt-pointed instrument a red reaction along the line of pressure is visible 3 to 15 seconds after the application of the pressure. It reaches its height in half to one minute, and fades gradually in a short time. In persons with hyper-sensitive skin the reaction to such a stroke does not stop at the red line, but this red reaction is followed by a local swelling of the skin, i.e., a weal. This condition of the increased susceptibility of the skin to mechanical stimuli is called urticaria factitia or dermographia. As a result of this increased susceptibility letters and words can be written on the skin by scratching with a finger nail or by stroking with a blunt-pointed instrument.

Ætiology.—(1) Both Lewis (1927) and Krogh (1929) put down dermographia to an exaggerated normal reaction of the skin to injury. They believe that all weals, including the factitious weal, are the result of a common chemical substance (which is released by injury to tissue cells) and that the substance exerts a local action upon cutaneous vessels and nerves. The action of this substance is indistinguishable from that of histamine and Lewis called it an H substance. This H substance calls forth the local vascular reaction which terminates in a weal—the triple response of Lewis. This triple response includes, (a) local dilatation of the finest vessels, (b) the flare which is a widespread dilatation of the neighbouring arterioles, and (c) local œdema or weal due to increased permeability of the vessel wall. They contend that the constituent parts of the triple response cannot be attributed directly to the physical stimulus and produce evidence to the effect that a diffusible substance is liberated in the skin which is responsible for the local reaction by its direct effect on the vessel wall and which yields a widespread arteriolar dilatation by acting on a local nervous mechanism. Lewis presents numerous arguments to show that this H substance

simulates histamine more closely than any other substance employed for production of weals. (2) He found that the fluids obtained from the weals of the skin produced by stroking or from small blisters due to burns could stimulate the guinea-pig's uterus to strong contraction, like histamine in great dilution. (ii) Lewis, by producing a large number of these weals on the bodies of patients with urticaria factitia, was able to produce certain constitutional symptoms, such as a rise of cutaneous temperature, flushing of the face, and a slight fall of blood pressure. He argued that the injury at many sites at the same time released considerable quantities of H substance in the wealed areas and that



the constitutional symptoms were due to this substance which had escaped from these areas into the general circulation. Since these symptoms correspond closely to those resulting from subcutaneous injections of minute doses of histamine, he concluded that the action of histamine and H substance were identical. (iii) Harris, working in Lewis' laboratory, showed the presence of a histamine-like substance in alcoholic extracts of human skin. Best, Dale, Dudley and Thorpe (1927) had already demonstrated and isolated histamine from the lung and liver tissue. Barger and Dale (1910) first isolated histamine in pure form from the mucous membrane of the bowel.

Histamine may be in the cell potentially in the form of some inactive precursor, or it may be present in the cell interior, and, being prevented from leaving it so long as the cell membrane is physiologically intact, it produces its action only if some stimulus or injury causes its escape into the extra-cellular fluid.

Krogh quite agrees with Lewis' hypothesis but thinks that the evidence points rather definitely to the existence of at least two substances; one of these is histamine-like or histamine itself, which possesses a relatively small molecule and is readily taken up by the blood through the capillary wall, and the other substance is a colloidal substance of complex nature and of very low diffusibility. Lewis and Krogh both believe that exaggerated reaction to stroking in subjects of dermatographia is not due to increased susceptibility of the mechanism of the reaction to stimulation. Lewis finds that in urticaria factitia the skin is hyper-sensitive to stroking, but if histamine is punctured into the skin the resultant weals are no larger than in controls similarly tested. He argues that if the proneness of urticarial subjects to flare and to weal consists of an unusual reactivity of the vessels, then the stroke and histamine would both be expected to yield exaggerated reaction; in actual experience they do not, response to stroke alone being conspicuous. But our case demonstrates that in urticaria factitia response to histamine is increased. Lewis says that a puncture through solutions of histamine of lower concentration than 1/1,000,000 brings the same result as a puncture through saline. We did not try the puncture test, but in our case the dermal test was positive in a dilution of 1/2,000,000 and lower dilutions were not tried. This result can be compared with the results obtained in 15 asthma patients who were tested up to a dilution of 1/20,000—

8 cases were positive in 1/20,000 dilution,
4 cases were positive in 1/10,000 dilution,
3 cases were positive in 1/8,000 dilution.

So that in our case of dermatographia the reaction to histamine is increased.

Working on the basis that reaction to histamine in dermatographia patients is not increased Lewis concludes that susceptibility of the skin of the urticarial case is really a susceptibility of its cell elements to mechanical injuries, for example, an unusual fragility, or possibly a departure from the usual grade of metabolic stability upon the receipt of these forms of minor damage.

Krogh states that the amount of histamine set free by a given stimulus is evidently very variable and the large variations in susceptibility of individuals and species to different forms of tissue injury are largely to be explained as variations in histamine production and only to a minor, but unknown extent, as variations in reactions to histamine. Thus, to summarize,

both Lewis and Krogh place dermatographism in line with exaggerated normal reactions of the skin to injury. According to their view a mechanical stimulus produces more histamine in an urticarial subject than in an ordinary subject, and that the urticarial subject reacts more strongly by virtue of the greater amount of histamine set free. This setting free of greater amount of histamine is due to greater susceptibility of the cell elements to injury in the shape of unusual fragility, etc. We have already mentioned that our case exhibited a stronger reaction to histamine than normal individuals so that we cannot accept that the whole of the difference in susceptibility to injury of urticarial patients is due to the difference in the amount of production of histamine and not to any difference in susceptibility to histamine.

(2) Walzer (1928) takes objection to the position taken up by Lewis and Krogh, and states that dermatographism is a pathological condition and not an exaggerated normal one. He is inclined to the view that the presence of dermatographism indicates some general internal pathologic process. He stroked the skin of the backs of 48 persons, cases of mild skin diseases, and as controls, of thirteen subjects with urticaria and pruritis. Out of the 48 only 11 responded with a weal after from eight to twelve consecutive strokes over the same area; all the weals were mild, some extremely so, and could be felt rather than seen. Out of 13 patients with urticaria and pruritis 11 responded with a weal on a single stroke only. The poorest reaction in this group was much more pronounced than the best reaction in the previous group.

He next tried if urticaria factitia could be experimentally produced by injecting the serum of a dermatographic patient into the skin of a normal person, and then stroking these sites of injection. He used sera of 10 dermatographic cases and each serum was injected into at least 5 or 6 different persons. A dermatographic state was produced on the skins of non-dermatographic subjects with the serum of only one of the dermatographic patients. From this he concludes that although the presence of a transferable dermatographism-inducing principle in the blood stream of an average patient with symptoms of urticaria factitia cannot be demonstrated with this technique, its existence cannot be excluded as it is possible that in the blood of the average patient it may be in too high a dilution to manifest itself by this procedure.

Walzer contests the assertion of Lewis that all weals are fundamentally the result of a common causative factor—'a liberated substance or substances having a histamine-like action'. Injection of the serum of a patient in whom a dermatographism-inducing principle could be demonstrated did not produce any weal at the time of injection, but it induced a state of altered reactivity so that trauma at a subsequent date produced a dermatographic response.

Had this dermographism-inducing principle been like Lewis' H substance the injection of the serum into normal skin should have induced a histamine weal at once.

Description of the case.—An Indian male, aged 20, suffering from dermographia for the last two years. No history of urticaria or other skin allergy in the family.

Blood count.—Total leucocytes 20,000 per c.mm.

Total eosinophiles 1,000 (5 per cent) per c.mm.

Large mononuclear 400 (2 per cent) per c.mm.

Lymphocyte 3 per cent.

Polymorphonuclears 63 per cent.

Blood calcium 0.0098 per cent, or 9.8 mgms. per 100 c.cm.

Histamine dermal test.—Positive with 1/2,000,000 dilution—negative with 1/20,000,000 dilution.

Intra-dermal test.—Positive with 1/20,000,000 dilution, lower dilution not tested.

Desensitizing with histamine.—Desensitization was started with 0.1 cubic centimetre of 1/20,000,000 dilution. The dosage was gradually increased and a maximum dose of 0.3 cubic centimetre of 1/2,000 dilution was reached on the fourth day. On the fifth day the dermal and intra-dermal tests with histamine were repeated with the following results:

Dermal test.—Negative with 1/20,000 dilution, higher dilution not tried. (On the first day the test was positive with 1/2,000,000 dilution.)

Intra-dermal test.—Positive with 1/2,000,000 dilution, negative with 1/20,000,000 dilution. (On the first day positive with 1/20,000,000,000 dilution.)

Discussion

(1) Lewis and Krogh believe that hyper-sensitiveness of the skin of an urticarial case is really a susceptibility of its cell elements to mechanical injuries whereby a greater amount of histamine is produced than normally. There is a good deal of evidence that urticaria factitia can be produced by local changes in the tissue cells alone. Walzer and Walzer (1928) showed that stroking some of the sites of previous experimental weals reproduced weals at these sites a few days later. Similar trauma, applied to any other part of the surface of the skin at the same time, resulted only in the usual erythematous response, demonstrating the fact that the reaction was purely a local one. Fulleborn (Walzer, 1928) found that weals resulted from the penetration of stronglyloid larvæ into the skin. Stroking these particular areas within 2 or 3 weeks after the weals had gone, he elicited weals at these sites. Bettmann

(Walzer, 1928) demonstrated urticaria factitia over tattooed areas in a series of about forty-one patients. The subjects were not dermographic and had never had any urticaria. Rubbing or stroking the tattooed areas reproduced the outlines of the tattooed figures in weals.

(2) Lewis does not give any place to the increased reaction to histamine in the causation of urticaria factitia, as he finds that dermographic subjects are only sensitive to histamine to the same extent as a normal person. Krogh, although believing that the variations in susceptibility of individuals to different forms of tissue injury are largely to be explained as variations in histamine production, does not forget that they may be to a minor but unknown extent due to variations in reactions to histamine. The reaction to histamine in the case of dermographia described by us clearly shows that increased reaction to histamine plays some part at least in bringing about dermographism.

(3) That a dermographism-inducing principle circulates in the blood of at least some cases of dermographism is quite evident from Walzer's case in which he produced a dermographic state on skins of non-dermographic subjects by injecting the serum of a dermographic patient. Moreover we have seen dermographism in cases of filarial infection. We believe that in dermographism we have to deal with all these factors—(i) abnormal state of the tissue cells, this may be inherited or acquired as in Walzer's, Fulleborn's and Bettmann's cases, (ii) increased reaction to histamine, and (iii) the presence of some general internal pathological process. We have no evidence to show, but it is very probable, that this third factor works in association with decrease in pituitary hormone which Krogh has shown is responsible for maintaining the tone of the capillaries. It is quite conceivable that on account of deficiency of this hormone the permeability of the capillaries is increased, and that the toxin, whatever it is, can penetrate the capillaries more easily and that its action on the tissue cells is more apparent, making them hyper-sensitive to injury and the H substance.

REFERENCES

- Barger, G., and Dale, H. H. (1910). B-Iminazolyethylamine, a Depressor Constituent of Intestinal Mucosa. *Journ. Physiol.*, Vol. XLI, p. 499.
- Best, C. H., Dale, H. H., Dudley, H. W., and Thorpe, W. V. (1927). The Nature of the Vasodilator Constituents of Certain Tissue Extracts. *Ibid.*, Vol. LXII, p. 397.
- Krogh, A. (1929). *The Anatomy and Physiology of Capillaries*. London: Humphrey Milford.
- Lewis, T. (1927). *The Blood Vessels of the Human Skin and their Responses*. London: Shaw and Sons.
- Walzer, A. (1928). Experimental Urticaria Factitia. *Arch. Dermat. and Syph.*, Vol. XVIII, p. 868.
- Walzer, A., and Walzer, M. (1928). The Experimental Weal produced on Normal Skin through Internal Channels. *Ibid.*, Vol. XVII, p. 659.

MORPHINE HABIT IN INDIA

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In a previous paper (1928) the senior author stated that addiction to purified alkaloids of opium was a rare occurrence in India. In western countries morphine and of late years codeine and heroin also have been extensively used. In view of the fact that habitual use of alkaloids, such as cocaine, is being gradually introduced into India from these countries and from the Far East, the Drug Addiction Inquiry has been keenly on the lookout for extension of the morphine habit or habitual use of any of the other alkaloids of opium in this country. During the course of our field work in Northern India recently we have seen quite a number of cases of addiction to morphine, though not to codeine and heroin. Further enquiry into the matter elicited the fact that habitual use of morphine had undoubtedly increased in certain parts of India during the last few years. The increase at present is very small and only a few areas here and there are affected, but there appears to be a grave danger of its extension, if steps are not taken to meet the evil.

Source of supply.—Instances of the abuse of morphine were undoubtedly met with in the past, but these were uncommon. Further the drug was almost always taken by the mouth, but lately we have seen many instances where the alkaloid is being taken by injection; this increases the danger of the habit for reasons discussed later. In spite of the vigilance of the excise authorities there appears to be no difficulty in procuring the drug for euphoric purposes. We have been informed by the addicts themselves that the alkaloid can be bought in any of the large towns in Northern India without difficulty. The following are some of the avenues by which the drug finds its way to those addicted to its use:

(1) The use of morphine appears to have been encouraged and the alkaloid obtained through the agency of 'medical practitioners' who are holding licenses to stock and dispense this drug. The law in this country as regards registration of medical practitioners is not strictly enforced and there are numbers of unqualified persons practising in almost every town and village, who are not borne on the medical register of the different provinces. Some of these individuals have managed to get licenses to keep morphine for sale and they have been abusing the privilege. A careful

examination of the daily sales-register of one such licensee showed that morphine in the guise of prescriptions was being regularly sold to a number of people throughout the year. Out of 200 legal sales by this person during the year 1931-32, there were none below 1 grain, i.e., about 4 times the usual therapeutic dose. The following is a sample of the prescriptions written by one 'practitioner':—

Liq. ammon. acetat	..	4 drachms.
Spt. ammon. aromat.	..	4 "
Sod. bicarb.	..	3 "
Pot. iodide	..	1½ "
Syrup tolu	..	1½ "
Morphine sulph.	..	12 grs.
Aqua chloroform.	..	12 oz.

Dose—1/12th part to be taken 3 or 4 times a day, or

Morphine sulphate 24 grs.

Divide into 12 powders.

The alkaloid was shown to be prescribed in the treatment of asthma, abdominal troubles (diarrhoea and colic), insomnia, joint pains, etc., but it was really being given to persons who had formed the habit and were addicted to the drug. Some of these licensees are addicted to morphine themselves and play a part in developing the habit in others and disseminating the use of the drug by telling people of the wonderful effects produced by it in various conditions.

(2) Besides obtaining the drug by false prescriptions there is another source from which the supply of morphine comes into the hands of addicts. We have been informed that there is some leakage from large hospitals and medical institutions, and a certain amount of the drug is stolen and sold to dealers who pass it on to the addicts.

(3) The drug has also been obtained through apparently legitimate sources. In one of the towns we found that a number of addicts were taking large doses of morphine daily and were getting the drug from the license holders in the ordinary way. Their names were borne on the register of the excise authorities and they were issued with regular permits to buy their daily rations.

Careful inquiries in various places showed that the drug was not being smuggled from foreign countries as is the case with cocaine. This is due to the fact that at present there is a small demand for it and it is not worth the while of the smugglers to be interested. If, however, the habit spreads more the smuggler will become interested and will try to push the contraband trade.

Morphine habit among Indians

(1) *Euphoric use.*—It has been possible for us to study quite a number of persons addicted to morphine. The causes which lead to this addiction among Indians do not differ from those producing other drug habits. The habitual use of morphine in this country resembles

the cocaine habit as described by Chopra (1931). The habit is very seldom started for its sedative and analgesic properties as it is in western countries, but indulgence is practically always started on account of the sense of euphoria that it is said to produce. Persons, taking narcotic drugs habitually, often extol their virtues and relate the wonderful effects produced by them to their credulous friends. The types of individual most attracted by such descriptions are young persons between the ages of 20 and 35 who are induced to try the drug entirely for production of euphoria. Sexual factors also play a very important part so far as this class is concerned. The majority of these addicts believe that morphine has remarkable power as an aphrodisiac, and in quite a large number of cases they started using the drug for this reason. The alkaloid is at first used occasionally and the fact is kept secret. Repeated use of the drug however quickly leads to habit formation and these young adults become slaves to the habit. The stage is soon reached when morphine is the only drug which relieves them of their imaginary mental and physical troubles.

Psychopaths and neurotic individuals are particularly prone to contract the habit and one dose of the drug leads to a great craving for another, and the dose is rapidly increased. Most of the morphine addicts we have met in India have belonged to these two groups. Although the large majority of those seen by us were males, we have been credibly informed that the habit is not uncommonly met with among the females of certain classes in large towns.

(2) *For the relief of pain.*—Although the morphine habit in western countries, in a very large majority of cases, is started after its use for relief of bodily pain, this appears to play very little part so far as the Indian addicts are concerned. In fact in the series of cases we have studied there was not a single individual whose habit could be directly assigned to the use of the drug for bodily pain, either on the advice of a medical man or by way of self medication. Our experience is that opium and morphine are prescribed to a much smaller extent by the Indian practitioners than by their confrères in the west. The use of the drug for relief of pain, fatigue, insomnia, etc., has only rarely given rise to the habit. Such addicts are as a rule persons of middle age and very often they are aware of the harm the habitual use of the drug is doing them and therefore increase the dose very gradually.

(3) *As a substitute for opium or to cure opium habit.*—We have met a number of instances where people taking large doses of opium have resorted to the use of morphine, hoping that this will enable them to cut down the quantity of their opium consumption. Some have gone so far as to hope that this would rid them of the opium habit. The result often

is that not only do the addicts not succeed in getting rid of the opium-eating habit, but they begin to take morphine in addition to the usual quantity of opium. Persons interested in the sale of morphine often urge that it is cheaper to replace opium with morphine and that there is less likelihood of forming a habit with it, but this is a deliberate falsehood. Such statements have however been responsible for producing the morphine habit in quite a number of ignorant persons.

Modes of administration.—Morphine is taken by the Indian addicts in two ways :

(1) *By the mouth.*—This was the method which was used almost exclusively till a few years ago. The reason was that it was often used as a substitute for opium and the addicts preferred to take it in exactly the same way as they did opium. When the drug is taken in this way the effect of the dose is prolonged, but it is not so lasting as opium because its absorption from the gut and its excretion are much quicker.

(2) *By injection.*—The difficulty of performing the operation of injection, which requires some skill, has stood in the way of this method being used to any great extent in the past. It has however come into vogue recently and during the course of our work in the field we have encountered instances of this method of administration of the drug amongst the laity. Septic infection and even death from tetanus have resulted among addicts. The advantage of this method, from the addicts' point of view, is that the effects are almost immediately obtained and are more intense, but the disadvantage is that duration is much shorter. In consequence there is greater desire for the repetition of the dose and the abstinence symptoms are much more intense.

Dosage.—The average dose of the alkaloid taken by the addicts in our series is between 4 to 6 grains daily. The common practice is to take it in the morning and evening whether by injection or by mouth. There is a great tendency towards increasing the dose among the addicts who take it to produce euphoria and in neurotic individuals. We have found persons taking as much as 10 to 20 grains a day. A case was reported from the North-West Frontier Province in which as much as 60 grains a day were taken by injection.

Age and duration.—In the majority of cases studied the habit was said to have been contracted between 18 and 35 years of age. Addiction to opium, on the other hand, is more commonly seen in persons after the age of 40, it being essentially a habit of middle age. In the areas where a large number of addicts were seen, in the majority the habit had not lasted for more than 4 or 5 years. Practically all the addicts who practised injection had been doing it for less than six years. A few addicts who took morphine by the mouth said they had

done so for 10 to 15 years, but such long duration was uncommon. Evidence at our disposal points to the fact that the pernicious type of addiction is to be met with only amongst the youths in this country, it is of recent origin and has only developed during the last 5 or 6 years at the most.

Symptoms and effects.—Chopra and his collaborators have fully discussed in a series of papers (1927—1932) the effects produced by the opium habit among Indians. During our study of the present series of morphine addicts we tried to observe if there were any marked differences in the symptoms and effects produced by the two drugs, opium and morphine. So far as the immediate effects of taking morphine by the mouth are concerned, these do not differ materially from those produced by opium except that the onset perhaps is more rapid. A dose of opium taken by the mouth usually takes 10 to 15 minutes before its effects are manifested whereas morphine taken by the mouth takes 5 to 10 minutes. The effects of injection are however manifested within a few minutes and the feelings of elation and euphoria are much more pronounced after an injection.

In their later effects opium and morphine whether taken by the mouth or by injection differ a great deal and we will refer to these differences briefly. The physical examinations carried out in a number of cases showed that most of the habitués were well-built, but they all looked pale and anæmic. The pulse and respiration were rather slow, the blood pressure was below normal and the pupils were generally contracted. The tongue was thickly coated and the bowels were constipated. As already stated morphine is habitually used in India almost entirely for its euphoric effects and for sexual gratification by young and middle-aged persons. Opium as a general rule is taken habitually by the older people and generally for disease and old age. The morphine habitué shows the physical effects much more rapidly than the opium addict. Within a year or so the former becomes pale and emaciated, and begins to suffer from symptoms of cachexia. Opium addicts, even those taking moderately large doses, go on for many years before they show any apparent signs of degeneration. Morphine addicts soon become physical wrecks while opium addicts take a long time to reach this stage. The blood pressure is perceptibly lowered in morphine addicts while in opium addicts no such effect is produced.

When under the influence of morphine the addict looks worried, depressed and hypersensitive, whereas after a dose of opium he is cheerful, care-free and talkative. Persons taking small doses of opium carry on their work quite well, but those taking even small doses of morphine are unable to concentrate and show a general lack of responsibility. There is impairment of memory, and judgment is

disturbed. Mental and moral deterioration sets in more rapidly and is much more marked in morphine addicts, who will often commit criminal offences. In opium addicts mental deterioration occurs much more gradually and only when large doses are taken. Abstinence symptoms are much stronger among morphine habitués than in those addicted to opium and there is also a greater tendency for the dose to be increased. The morphine habit is much more difficult to break than even the opium habit.

Summary and conclusions.—Habitual use of morphine has increased in India during the last few years. The increase at present is small and only a few areas here and there in Northern India have been affected. There appears, however, to be grave danger of its extension, if steps are not taken to check it.

The habit in India is usually met with in young persons between the ages of 20 and 35 years. The habitual use of morphine in this country resembles the cocaine habit to a great extent. The habit is not started for its sedative and analgesic effects as in western countries, but for its euphoric effect and because of its supposed aphrodisiac properties. Formerly the alkaloid was taken almost exclusively by the mouth but recently the injection method has come into use.

Various factors in connection with the types of addicts, the dose taken, duration of the habit, comparative effects produced by opium and morphine habits among Indians have been discussed.

REFERENCES

- Chopra, R. N. (1928). The Present Position of Opium Habit in India. *Indian Journ. Med. Res.*, Vol. XVI, p. 389.
- Chopra, R. N. (1930). A Preliminary Note on Addiction to 'Post' (Unlanced Capsules of *Papaver somniferum*). *Indian Med. Gaz.*, Vol. LXV, p. 361.
- Chopra, R. N., and Bose, J. P. (1930). The Action of Opium in Diabetes. *Indian Journ. Med. Res.*, Vol. XVIII, p. 15.
- Chopra, R. N., and Bose, J. P. (1931). Effect of Opium on the Blood-Sugar of Non-Diabetics. *Indian Journ. Med. Res.*, Vol. XVIII, p. 1087.
- Chopra, R. N., and Bose, J. P. (1931). Opium and Albuminuria. *Indian Med. Gaz.*, Vol. LXVI, p. 299.
- Chopra, R. N., and Bose, J. P. (1931). Psychological Aspects of Opium Addiction. *Indian Med. Gaz.*, Vol. LXVI, p. 663.
- Chopra, R. N., Bose, J. P., and De, N. N. (1931). Further Observations on the Effect of Opium on Blood-Sugar. *Indian Med. Gaz.*, Vol. LXVI, p. 625.
- Chopra, R. N., and Chopra, G. S. (1931). Cocaine Habit in India. *Indian Journ. Med. Res.*, Vol. XVIII, p. 1013.
- Chopra, R. N., Chopra, G. S., and Grewal, K. S. (1932). Opium Habit in the Punjab. Part I. *Indian Journ. Med. Res.*, Vol. XX, p. 545.
- Chopra, R. N., and Ghose, N. N. (1931). Addiction to 'Post' (Unlanced Capsules of *Papaver somniferum*). Part II. *Indian Journ. Med. Res.*, Vol. XIX, p. 415.
- Chopra, R. N., and Grewal, K. S. (1927). Opium Habit in India. Analysis of 100 Cases amongst the Sikh Population of Calcutta. *Indian Journ. Med. Res.*, Vol. XV, p. 57.

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SOME FACTORS REGULATING METASTASIS IN CARCINOMA AND THEIR INFLUENCE ON PROGNOSIS

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It is a general rule that when a malignant epithelial neoplasm grows in any part of the body the tumour cells tend to burrow their way into the lymphatic spaces and spread along these channels. Hence extension and dissemination of the growth take place along the lymph channels. Sooner or later, however, some of the atypical cells reach the general circulation through the thoracic duct. In the circulation they may either be dissolved by the cytolytic action of the blood or they may reach the lungs through the pulmonary artery and act as emboli, which may be the starting points of metastatic nodules.

Before the cells can reach the general circulation, they must pass through lymph nodes, which are thus involved one after another. In the lymphatic glands the tumour cells get ample nourishment, and consequently multiply very rapidly and produce masses of growth which ultimately replace the parenchyma of the glands and cause various grades of glandular enlargement. Towards the beginning, these glands act as efficient filters preventing the onward passage of the neoplastic cells, but when the gland tissue is considerably replaced, this protective power goes and the cells then begin to pass into the next group of glands, *via* the intervening lymph channels.

It is thus evident from the above well-established facts that, for the dissemination of a carcinoma, the integrity and potency of all the lymph channels are essential factors. If therefore these channels are obliterated, as sometimes they are, by a chronic sclerosing type of lymphangitis, it becomes difficult for the cells to pass into and reach the proximal lymph nodes. The carcinoma will, in that case, have no other alternative but to grow locally, and extend by local tissue destruction. The inception of this factor in the course of the neoplasms will have a significant bearing on the duration of the disease which may be prolonged for

many years. The following interesting case may be cited as an illustration:

Case report.—An adult, Hindu male, aged 35 years, a carpenter by occupation, noticed a swelling the size of a marble on the left scapular region in 1923. It continued to grow, rather slowly at first, till it burst, forming an ulcer, which failed to respond to ordinary treatment. Two years passed, the ulcer increased in size, and the patient sought for relief in the hospital.

Condition on examination (*i.e.*, in 1925): The ulcer area was 3 by 5 inches in size, and presented a very foul-smelling ulcerated area covered with patches of slough. The entire mass was firmly fixed. The character of the surface, base, and edges suggested a typical cauliflower-like carcinoma. A piece of tissue removed from the edge proved, on histological examination, to be epidermoid carcinoma. A thorough clinical search failed to reveal any glandular involvement. Considering the lymphatic drainage of the parts one would have expected the subscapular group of the axillary set of lymphatic glands to be enlarged, but such was not actually the case.



Fig. 1.

Operation.—A complete excision of the ulcer with all suspicious tissues and scraping of the scapular group of muscles were undertaken. A very large bare area was produced which took a long time to heal, ultimately requiring skin-grafting. The patient was under observation for nearly three months, but made a complete recovery.

After-history.—The patient had no trouble till 1930, *i.e.*, after the lapse of 5 years, when he noticed a swelling in the same region. This also burst and an indolent ulcer was produced. He came again under observation in 1933. The condition on admission may be realized from the photograph (figure 1). The growth measured

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Chopra, R. N., Grewal, K. S., Chowhan, J. S., and Chopra, G. S. (1930). Addition to 'Post' (Unlanced Capsules of *Papaver somniferum*) in India. *Indian Journ. Med. Res.*, Vol. XVII, p. 985.

Chopra, R. N., and Knowles, R. (1930). The Action of Opium and Narcotine in Malaria. *Indian Journ. Med. Res.*, Vol. XVIII, p. 5.

Chopra, R. N., Mukherjee, B., and Dikshit, B. B. (1930). Narcotine: Its Pharmacological Action and Therapeutic Uses. *Indian Journ. Med. Res.*, Vol. XVIII, p. 35.

8 inches by 6 inches. The edges were everted and indurated, and the base fixed to the underlying tissues. A very careful search on this occasion again failed to reveal any enlargement of the lymphatic glands. Nor was there any clinical evidence of metastases anywhere else in the body, except a swelling on the adjacent part of the posterior aspect of the middle of the arm which was evidently due to local extension. The lungs were normal but no skiagram could be taken as the patient suddenly left our hospital. Although the scapula was movable, there was some limitation of movement of the shoulder joint obviously due to adhesions and loss of muscle tissue.

Discussion.—It seems probable that the growth originated in a sebaceous gland, either as a primary condition or as a secondary superimposed condition brought about by irritation of an ulcer by the application of the irritating country medicines. Whatever might be the



Fig. 2.

origin, there was no doubt that it was a malignant growth and as such should have involved the proximal lymph nodes by metastasis. But, on both the occasions when the growth was examined, the lymph glands were found to be conspicuously free. The malignancy of the epidermoid group of carcinoma may not be very great, when compared with the carcinoma of the breast or alimentary tracts, but early glandular involvement of the part affected is the usual feature.

This would suggest that either the cancer cells could not reach the glands through the lymphatic channels which were rendered too narrow for the passage of the comparatively big squamous cells, due to some sort of obliterating lymphangitis, or that the cells, although they reached the glands, could not grow and multiply owing to the early development of

cytolytic factors. Ulceration in an exposed part in an illiterate patient with little sense of cleanliness might have induced sufficient inflammatory reaction to cause occlusion of the lymph channels in the surrounding areas. Moreover it is definitely known that the growth of a carcinoma and the infiltration of carcinoma cells in the tissues sometimes excite a very marked proliferative tissue reaction in the neighbouring areas; such chronic inflammation may often produce a barrier to the further extension of the growth by the deposition of fibrous tissues, as is very well known to occur in the case of scirrhus carcinoma of the breast of long duration. Another effect of such long-continued inflammation may be the formation of many foreign-body giant cells, which are set up against the invading carcinoma cells causing their ultimate destruction (*see figure 2*). The result of the action of all these has been that the growth has remained strictly local, and its malignancy consequently has also been a local one. The outcome of such alteration is not without its value to the patient, for it not only gives a longer lease of life to him by preventing a generalized dissemination, but also presents a very suitable local condition for complete cure by modern surgical methods, such as excision by diathermy alone, or combined with the application of accessory therapeutic agencies, such as x-rays and radium.

But when we consider that even after a complete excision with sufficient healthy areas to ensure a thorough removal there was a recurrence, it becomes rather difficult to understand why the growth should be mild enough to leave the lymph nodes of the parts untouched.

It will be seen that the total duration of the carcinoma from the time of its first appearance to the time the man came under observation for the second time was ten years, and that during all this time it remained only locally malignant. We looked into the references at our disposal, but could not find any record of an epidermoid carcinoma remaining only locally malignant in spite of its power of recurrence during such a prolonged period as ten years.

Summary

Metastasis in carcinoma usually takes place through the lymphatics, but, in the late stages, it may be through the general circulation. Involvement of the proximal lymph nodes within a reasonable period is the rule.

Occlusion of lymph channels by inflammatory changes prevents the extension of malignant epithelial growth into the lymph glands and prevents their enlargement.

For the same reason such growths remain locally malignant and can only extend centrifugally by local destruction of tissues.

(Continued at foot of opposite page)

MIXED TUMOUR OF THE FACE, NOT ASSOCIATED WITH THE PAROTID GLAND

By P. N. RAY, B.A., M.B. (Cal.), F.R.C.S. (Eng.)

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A MIXED tumour of the face unconnected with the parotid salivary gland is of sufficient rarity to warrant the detailed study of a single case. Additional interest is attached to the following case because the greater part of the tumour was composed of a large single translucent cyst. In this brief review, an attempt has been made to summarize the essential features of the few cases that it has been possible to collect from the literature.

The present case

S. B. G., Bengali female, aged 18, married. (First examined by me on 2nd October, 1932.)

History.—A small rounded painless nodule about the size of a pea was noticed three years ago, over the left side of the face. Originally of slow growth, the tumour rapidly increased in size to that of a walnut, during the last five or six months.

No other member of the family was affected.

On examination.—The tumour was situated over the left side of the face about half an inch in front of the lobule of the ear and about an inch above the lower border of the body of the mandible. The overlying skin was telangiectatic and adherent to the tumour for an area half an inch across. No punctum could be discovered. The tumour was smooth, rounded, fluctuant and translucent. It was freely movable over the deep fascia.

Corresponding cervical lymphatic glands were not enlarged. No other tumour was present on the body.

Operation was postponed on account of seabies from which the patient was then suffering, and she had a subsequent attack of influenza.

Two months later.—The tumour increased to a diameter of nearly 2 inches. On operation, a clear fluid of a pale yellow colour was withdrawn. On microscopic examination, neither epithelial cells nor cholesterol crystals were found.

Operation.—The tumour was excised under local anaesthesia with all the adherent skin, and a free margin of healthy tissue. It was surrounded on its deeper aspect by a sort of fibrous capsule. There was neither any adhesion to the deep fascia nor any connection whatever with the parotid gland.

Macroscopic appearances.—The tumour, submitted for examination, was covered with intact epidermis. It was placed in a hardening solution, containing formalin, whereby the fluid contents of the large cyst were converted into a homogeneous transparent jelly. On section, the inner lining of the cyst was smooth, but

intracystic projections were present on the floor. The cyst, forming the greater part of the tumour, was situated beneath the superficial solid part, which was only about half an inch in thickness and presented a semi-translucent surface, mottled with whitish areas of denser growth.

Microscopic appearances.—The histological picture is a complex one.

(i) The continuity of the epidermis with the cells of the neoplasm cannot be traced anywhere, but telangiectasis is marked (figure 1).



Fig. 1.—Photomicrograph (low power). (1) Epidermis with telangiectasis. (2) Large cyst. (3) Solid part of the tumour.

(ii) The epithelial cells are arranged in columns, masses and in places in alveolar formation enclosing a homogeneous material, but the reproduction of the dermal glands is nowhere clearly attempted. In some places, the cells are small and compact with scanty protoplasm and hyperchromatic nuclei, resembling those of the basal-cell carcinoma (figure 2).

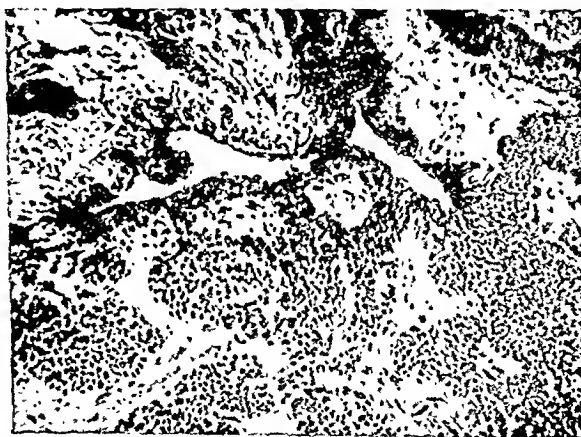


Fig. 2.—Photomicrograph (magnified). (1) Small cysts lined by basal cells. (2) Palisade arrangement of the outer layer of cells. (3) Connective tissue matrix showing hyaline change and cylinder formation.

There are also solid anastomosing strands or cords, with club-shaped prolongations of which

(Continued from previous page)

Such a pathological condition, of necessity, will very much prolong the duration of the disease and lengthen the life of the patient. It also provides the surgeons with a suitable opportunity for totally eradicating the disease.

A case has been described in detail, in support of the above observations; in this case the total duration of the disease was over ten years.

the outer cells are columnar and are arranged radially in palisade formation. Prickle cells are absent and so are keratinized 'cell-nests'. But numerous cystic areas are included among the larger cell masses. Some of the smaller cysts are lined by the basal cells (figure 2). Mitosis is infrequent.

In some places, the cells tend to become flattened and spindle-shaped and to form compact masses in which hyaline intercellular substance appears in increasing amounts. This appearance resembles that of the endothelioma (figure 3).

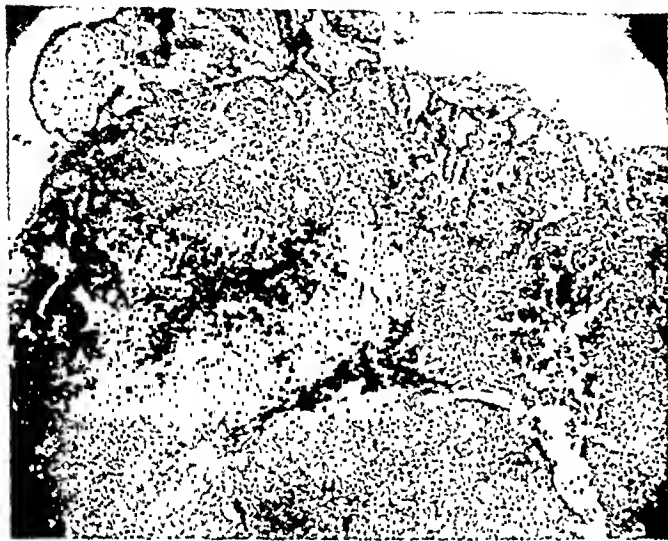


Fig. 3—Photomicrograph, showing the main tumour mass.

(iii) The supporting frame-work of connective tissue also presents a varied appearance. Between the epithelial masses, there is a fibro-vascular stroma, which resembles the corium with its capillaries. In places, it has undergone a hyaline change, but there are areas where a definite cystic change has occurred or



Fig. 4.—Photomicrograph (high power). (1) Intracystic papilliferous projections on the floor. (2) Cystic contents. (3) Roof formed by a compact mass of cells.

where cylinder formation is marked (figures 2 and 4).

(iv) The large cyst has a thin floor, formed by a few layers of well-staining cells of the squamous type. The roof, however, is formed by a compact mass of epithelial cells, which are continuous with the body of the neoplasm. In places, intracystic papilliferous projections are present, but these are not well marked. The cystic contents are homogeneous in nature, and are stained pink with van Gieson stain (figure 4).

Commentary

There has always been much dispute regarding the origin of the mixed tumours of the parotid region. According to McFarland (1927), only very few cystic tumours of this region have been described. He is of opinion that nearly all, if not indeed all, of the so-called adenomas are but mixed tumours of unusual appearance. In 1911, Vincent described a tumour of 24 years' duration as a cystic adenoma of the parotid, which, though of slow growth, rapidly increased in size during the last four years to a diameter of 10 centimetres. It was cystic and when punctured permitted the escape of sero-sanguinous fluid. Brunschwig (1931) has recently described a subcutaneous mixed tumour of the face, not associated with the salivary glands. Patey (1931) observes that the mixed salivary tumours are a composite group of epithelial tumours, the varying pathological features of which depend on the degree of differentiation attained and the rapidity of the division of the cells.

Discussing the theories of origin of these tumours in Choyce's (1932) *A System of Surgery*, Back states that the primitive and varied nature of the component cells is readily explained by the embryonic theory of origin. This view receives wide support at the present time, especially from the French writers. The tumours are supposed to be derived from islands of embryonic cells, sequestered during the development of the mouth and face, and included in or near the salivary glands, most commonly the parotid. This process has been called by them 'enclavement', and the new growth the 'enclavoma'. Regarding the encapsulated or extra-glandular type of new growths, Benedict and Meigs (1930) state, on the authority of Ewing, that these may take the form of a basal cell or adenoid cystic epithelioma. These probably arise from misplaced and occasionally embryonal portions of the gland tissue. Bronchial remnants may be connected with this group. These are, by many authorities, classed with the teratoid tumours. They consider that mixed tumours are essentially benign but recur locally with great frequency. These rarely become malignant.

McFarland (1926) has made the strong statement that nothing of prognostic value results from the microscopic study of a mixed tumour. These contain varying quantities of cellular tissue of different kinds. Among them are the so-called 'indifferent cells', which in their most primitive form resemble the short spindles of sarcoma. When the opinion that these cells were derived from the endothelium prevailed, they were thought to be a step to the sarcomata; but with the discovery that they are in all probability embryonal, epidermal and epithelial cells, their presence becomes of no significance with regard to the sarcomatous nature of the tumour in which they occur. Professor Kettle (1928) says that a highly malignant tumour, viz, the teratoblastoma, may occur in the parotid region. It is however a great rarity. The main mass of the tumour is composed of small rounded or oval cells of a distinctly sarcomatous type, lying in a loose oedematous or connective tissue matrix. Fry (1927) supports the view that these tumours are entirely epithelial in origin. Some of the tumours show varying degrees of malignancy. There is no definite dividing line between the innocent and malignant and some of the more malignant may show many of the features typical of the innocent type of tumours.

In this connection mention has to be made of the cylindroma, which is now regarded as a variety of endothelioma. Histologically, the cylindrical hyaline structures are seen to be formed by modification of the connective tissue stroma or of the walls of the blood vessels, although in some cases such hyaline masses appear to be found in the middle of the tumour cells. This has given rise to much confusion, as their structure is often seen in the basal-cell carcinomata. In a recent report of a case of cylindroma with multiple tumours of 17 years' duration, Nicolas, Massia and Lebeuf (1932) state that clinically the new growths appear to them to be benign but the histological picture is analogous to the basal-cell epithelioma. Borst (1922), however, has described a tumour of the skin, as an endothelioma derived from the lymphatic endothelium. The cells are smooth and flattened, and they form a net-work of solid strands and cords embedded in a connective tissue matrix. These cells show their primitive character in that they do not usually form the typical endothelial tubes as in the lymphangioma. Kaufmann (1929) is inclined to support the view of Krompecher that these are basal-cell tumours. A group of tumours of the skin, presenting the structure of cylindroma, was long regarded as endothelioma (Ewing, 1931). A typical case of this class and one much referred to is that of Braun. This tumour was shown by Krompecher to be of epithelial origin and is now generally grouped with the epithelioma adenoides cysticum of Brooke. It occurs in the form of nodular painless tumours of the skin, especially of the head and neck. These appear about the age of puberty and do not exceed the size of a pea or a bean. These tumours are derived from the basal cells of the epidermis and the hair follicles.

Ewing (1931), however, says that a single bulky tumour of similar structure may occur in the skin and the subcutaneous tissue about the face and the neck. Krompecher (1922), who introduced the term basal-cell carcinoma, speaks of the basalioma, or the cystic sebaceous adenoma, containing colloid cell cysts, which are comparable to those of the adamantinoma. According to him, this tumour also occurs on the face and is similar to the baso-cellular epithelioma and it may show, in parts, a cylindromatous or cystic structure.

Conclusion

The mixed tumour, described above, presents many interesting features. Basal cells are present and some of the smaller cysts are also lined by basal cells. It is known that the mixed tumour may take the form of a basal-cell tumour or the adenoid cystic epithelioma. But where the cell masses are more compact, the cells tend to assume a somewhat irregular form. Histologically the tumour has to be differentiated from the endothelioma. Every unusual tumour that lacks easily recognizable characters stands an excellent chance of being labelled an endothelioma. Further, the atypical endothelioma can scarcely be regarded as having an established position. It is true that in this case there is a tendency to cylinder formation, but it is a peculiarity which is seen in other tumours besides the cylindroma. The diagnosis of an atypical endothelioma is admittedly difficult. Professor Kettle (1928) has laid down the excellent dictum that the negative properties of a cell cannot demonstrate its origin, and it is only when the cells of a neoplasm present positive evidence of their endothelial nature that we are justified in calling the tumour an endothelioma.

With regard to the formation of the cystic spaces, two interpretations are possible, either these are due to degeneration of the stroma or these are the result of desquamation or the secretory activity of the cells of the neoplasm (Kaufmann, 1929). It is exceptional to find such a large cyst containing clear fluid.

There is no doubt that the varied natures of the component cells and the supporting stroma are readily explained, if the tumour is regarded as an 'enclavoma' of embryonic origin. The new growth (described above) is therefore diagnosed as a mixed tumour of the parotid region, of the extra-glandular variety.

Summary

1. A 'mixed tumour' of the parotid region, not associated with the parotid salivary gland, has been described.
2. The great bulk of the tumour is due to the presence of a single large translucent cyst, containing a clear fluid of a yellow colour.
3. Histologically, the varied nature of the component cells, the tendency to cyst and cylinder formation, and the infrequency of mitosis are noteworthy features.
4. The new growth has been diagnosed as an 'enclavoma' or a developmental tumour. It is possible that it has been derived from islands of embryonic cells, sequestered during the development of the face.

In conclusion, I wish to express my thanks to Dr. C. C. Bose, Professor of Pathology of the Carmichael Medical College, for his valuable help and suggestions, to Dr. D. N. Banerjee, for his help with the histological specimens and also to him and to Dr. P. C. Rakshit, for the photomicrography.

REFERENCES

- Benedict, W. B., and Meigs, J. V. (1930). Tumours of the Parotid Gland. *Surg. Gyn. Obstet.*, Vol. LI, p. 626.
- Borst, M. (1922). *Pathologische Histologie*, p. 310. Leipzig: Verlag von F. C. W. Vogel.
- Brunschwig, A. (1931). Subcutaneous Mixed Tumour of Face not associated with Salivary Gland. *Arch. Otolaryng.*, Vol. XIII, p. 52.
- Choyce, C. G. (1932). *A System of Surgery*, p. 147. London: Cassell and Co., Ltd.
- Ewing, J. (1931). *Neoplastic Diseases*, pp. 361 and 382. Philadelphia: W. B. Saunders Company.
- Fry, R. M. (1927). The Structure and Origin of the 'Mixed' Tumours of the Salivary Glands. *Brit. Journ. Surg.*, Vol. XV, p. 291.
- Kaufmann, E. (1929). *Pathology*, Vol. III, p. 2204. (English Translation). London: H. K. Lewis and Co.
- Kettle, E. H. (1928). *The Pathology of Tumours*, pp. 176 and 199. London: H. K. Lewis and Co.
- Krompecher, E. (1922). Zur vergleichenden Histologie der Basaliome. *Zeitscher. Krebsforsch.*, Vol. XIX, p. 1.
- McFarland, J. (1926). Ninety Tumours of the Parotid Region. *Amer. Journ. Med. Sci.*, Vol. CLXXII, p. 804.
- McFarland, J. (1927). Adenoma of the Salivary Glands. *Ibid.*, Vol. CLXXIV, p. 377.
- Nicolas, J., Massia, G., and Lebeuf, E. (1932). Cylindrome de la face et du cuir chevelu. *Bull. Soc. Franc. Dermat. Syph.*, Vol. XXXIX, p. 10.
- Patey, D. H. (1932). The Mixed Tumours of the Salivary Glands. *Brit. Journ. Surg.*, Vol. XVIII, p. 241.

PANTOCAINE IN EYE-SURGERY*

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Cocaine has so far held the field as the only satisfactory drug for surface anaesthesia in eye-surgery, but its toxic effect has always limited its use, and it is not often that the mydriasis and the slight paresis in accommodation that it produces are welcomed. Besides, the difficulty experienced in keeping an account of its use in conformity with the excise regulations has always made the eye surgeon long for a safer substitute. For these reasons, every surface anaesthetic that was put on the market was given an eager trial in this hospital, and we have now found pantocaine, which we have used on over 3,000 cases, to be an effective substitute for cocaine, with none of the disadvantages of the latter. Not being so toxic as cocaine, it also easily replaces novocaine for infiltration anaesthesia.

Para-butyl - amino-benzoyl - dimethyl-amino-ethanol hydrochloride, to give the full chemical name of pantocaine, is a whitish, odourless, crystalline powder, soluble in water. The solution stands any amount of boiling without decomposing and can therefore be sterilized easily, and it also keeps indefinitely without decomposition. In the presence of an alkali, however, the pantocaine base is precipitated in the solution. Its toxicity is just as low as that of novocaine, and is one-seventh that of cocaine. It is not a licensable drug.

Like cocaine, it paralyses the sensory nerve endings producing an anaesthesia of the superficial tissues of the eye, but it has no stimulant action on the sympathetic and hence the mydriasis and the contraction of the blood vessels seen in the use of cocaine are absent in

not injure in any way the tissues with which it comes in contact, including the corneal epithelium as well, provided of course the cornea is guarded from exposure and consequent drying.

There is a slight smarting when the first drop of the pantocaine solution is instilled into the conjunctival sac. It passes off in four or five seconds. The anaesthesia starts in fifty to eighty seconds, the time varying in different individuals. The effect of a drop lasts from eight to twelve minutes, but, when two drops or more are instilled with an interval of a few minutes between each instillation, the anaesthesia is prolonged and is more pronounced.

With a two per cent solution of pantocaine the anaesthesia comes on earlier, and is deeper and more lasting than with a one per cent solution. The one and two per cent solutions of pantocaine are as effective as the two per cent and four per cent solutions, respectively, of cocaine with regard to the depth of the anaesthesia, but with the former the anaesthesia starts earlier and lasts as long as with the latter.

The relative anaesthetic effect of cocaine and pantocaine was tried on 50 normal eyes. The comparison was made as far as possible on the same individual.

With a single drop of	THE ANAESTHESIA	
	Starts in about	Lasts about
Cocaine 2 per cent ..	100—120 sec.	6—8 min
Cocaine 4 per cent ..	90—120 "	7—12 "
Pantocaine 1 per cent	60—80 "	8—12 "
Pantocaine 2 per cent	50—70 "	10—12 "

The relative effect of the two drugs (pantocaine 2 per cent, cocaine 4 per cent) on the

	JUST AFTER INSTILLATION			3 HOURS AFTER INSTILLATION			AGE OF PATIENT
	Tension Schiötz	Reaction of pupil	Width of pupil	Tension Schiötz	Reaction of pupil	Width of pupil	Years
Right eye pantocaine 2 per cent.	20 mm.	Good	2½ mm.	20 mm.	Good	2½ mm.	20
Left eye cocaine 4 per cent.	20 "	"	2½ "	22 "	Sluggish	3½ "	
Right eye pantocaine 2 per cent.	22 "	"	3 "	22 "	Good	3 "	60
Left eye cocaine 4 per cent.	22 "	"	2½ "	28 "	Sluggish	5 "	
Right eye pantocaine 2 per cent.	35 "	Sluggish	3½ "	35 "	"	3½ "	35
Left eye cocaine 4 per cent.	35 "	"	3½ "	48 "	nil	6½ "	

pantocaine anaesthesia. Pantocaine has no effect whatever on intraocular tension; it does

pupil and intraocular tension on two normal-eyed people and in one glaucomatous case is shown above.

*Being a paper read before the Missionary Medical Conference held at Kodaikanal in May 1933.

The one per cent solution is used for all surface operations, such as removal of foreign

bodies on the conjunctiva or cornea, cauterization of corneal ulcers, and pterygium operations, and for the examination of photophobic eyes, and the two per cent solution for all intra-bulbar operations, such as cataract extraction, dissection and trephining.

As pantocaine has no effect whatever on the iris dilator or accommodative mechanism or intraocular pressure, it is an ideal drug for tonometry. One drop of the one per cent solution is enough for the purpose. The tonometer can be applied just a minute after the instillation.

In the fact that it has no deleterious effect on the corneal epithelium, pantocaine should have the preference over cocaine for all operative treatment of ulcers of the cornea.

For those who use a local anæsthetic for applying an irritant drug on delicate people, a half per cent solution is recommended. A drop or two of the two per cent solution injected under the muscles concerned, besides the drops on the conjunctiva, can be relied upon to give perfect insensibility for the muscle operations, such as recession and advancement.

As was mentioned above, pantocaine does not constrict the blood-vessel walls like cocaine; on the contrary, the smarting from the first drop of the solution causes a slight hyperæmia of the conjunctiva. So, for all operations, except perhaps the minor ones on the cornea, it is absolutely necessary to add adrenalin to the pantocaine solution to keep the operative field bloodless. We add two drops of the 1 in 1,000 adrenalin to each cubic centimetre of the pantocaine solution in whatever strength the latter may be used. The addition of adrenalin, besides inducing a local anæmia, augments the anæsthesia, making it more pronounced and more prolonged. It is possible that in some cases this pantocaine-adrenalin solution does not produce sufficient ischæmia, especially for cataract operations, and in such instances it may be necessary to instil a drop or two of the adrenalin 1 in 1,000 solution separately over the operative field.

For infiltration anæsthesia, pantocaine is used in 1 in 1,000 and 1 in 500 strengths; respectively, these are as good as, if not better than, the one and two per cent solutions of novocaine. Here also, the addition of adrenalin by two drops to each cubic centimetre of the fluid is essential for ischæmia and for increasing the intensity and duration of the anæsthesia.

Pantocaine can claim an advantage over novocaine in that the anæsthesia comes on earlier and is more lasting, and that the tenderness left behind in the parts infiltrated after the anæsthesia fades away is less. Incidentally, it is cheaper to use pantocaine in 1 in 500 strength than novocaine in two per cent or even one per cent strength.

Infiltration anæsthesia with	Starts in about	Lasts for about	Highest effect lasts for over
Novocaine 2 per cent with one drop of adrenalin to each c.c.m.	4-5 min.	2-3 hours	One hour
Pantocaine 1 in 1,000 with adrenalin as above.	5-9 "	1½ "	Half an hour
Pantocaine 1 in 500 with adrenalin as above.	3-5 "	5 "	Two hours

For orbital akinesia, for all operations of the lids and on the lachrymal apparatus, and for the retrobulbar ciliary block (which we use as a routine measure for most of the major intra-bulbar operations and for enucleation), we have found the 1 in 500 solution of pantocaine to give a uniform and perfect result, without in any way causing damage or irritation to the tissues infiltrated or producing any toxic effect.

We prefer to use the 1 in 500 strength to the 1 in 1,000 strength solution for the reason that the anæsthesia comes on earlier and lasts longer, though there is no difference in the depth of the anæsthesia in these two strengths.

Realizing the disadvantages attached to the use of cocaine for local anæsthesia, the medical profession has always wished for a substitute which is equally effective, but which at the same time is universally usable, relatively non-toxic and absolutely non-irritant in effect. While fulfilling these basic conditions for an ideal local anæsthetic, pantocaine can claim also to be comparatively cheaper, to be more stable in solution and to be more readily sterilized. To the eye surgeon, it further offers the advantage of not affecting in any way the pupillary width, the mechanism of accommodation, or intraocular tension, while keeping up the intensity and duration of the anæsthesia. Furthermore, pantocaine does not come under the purview of the Dangerous Drugs Act.

THE FREQUENCY OF HYDATID DISEASE IN INDIA

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In the past, references have been made by many writers to the comparative rarity of hydatid disease in human beings in India, although it is fairly common in sheep and is sometimes found in goats.

The reason usually advanced for the relative freedom of human beings from this disease is that the dog, the host of the adult tapeworm (*Echinococcus granulosus*), is not such a close companion of man in India as it is in countries where hydatid disease is prevalent. This fact no doubt plays an important part in limiting

the transmission of hydatids to man, but there are other factors which are also of probably considerable importance. The first of these is that in India animal food is not nearly so plentiful as in other countries such as Australia, a notorious focus of human hydatid infection, and so the viscera (liver and lungs) are more carefully preserved for human consumption here and are not casually thrown to the dogs, as they frequently are in Australia. The result is that Indian dogs do not have the same opportunities of acquiring the infection from sheep. Climate is probably also of some importance because hydatid disease is mainly one of temperate regions. This is well illustrated in Australia where it is much commoner in the cooler south than it is in the tropical and sub-tropical north of the continent, notwithstanding the fact that conditions of life and opportunities of acquiring the infection are approximately the same all over the pastoral areas. On the other hand it is doubtful if the few cases that find their way to the larger hospitals give a true indication of the frequency of this disease in India, and whether there are not many unrecognized cases in the country districts.

Regarding the infection rate in dogs in India no literature is available as far as I am aware, and the only figures I have are those obtained from the examination of one hundred pariah dogs of Calcutta that were killed and examined for parasites in my laboratory at the Calcutta School of Tropical Medicine two years ago. Only two of these dogs harboured the worm *E. granulosus*. Dew (1928) stated that in Melbourne, Australia, dogs employed by butchers, drovers and farmers at the municipal abattoirs were infected to the extent of almost one hundred per cent. These dogs of course represent a highly selected class, and he goes on to say that dogs in other parts of the city show a very low infection rate and he quotes Clunies Ross in Sydney who found no dogs infected out of one hundred strays that he examined. Apart from the exceptional group of dogs in Melbourne referred to above, infection is much commoner in the country than in the city. In the grazing districts it is widespread and Dew quotes Clunies Ross who found that in New South Wales the infection rate in dogs in these areas varied between fifteen and sixty per cent with a general average of eighteen per cent. Therefore considering these facts and figures together with the small chance that dogs in the city of Calcutta would have of acquiring the infection, but where two in one hundred have been found infected, it seems very probable that *E. granulosus* infection is fairly common in dogs in the country districts of India.

Direct means of ascertaining the true prevalence of infection, either in human beings or in dogs, are not at present available in India, but a recent paper by Mahadevan and Menon (1933) presents an opportunity of obtaining

some indirect evidence regarding human infections.

The commonest site of hydatid infection is the liver, and this is clearly shown in the following table copied from Dew (1928). The second column indicates the figures for India.

Table of distribution of primary cysts (after D  v  )

		Percentage in Indian cases
Liver	.. 76.6	50
Lung	.. 9.4	5
Muscles and cellular tissues	.. 5.2	5
Kidney	.. 2.3	5
Spleen	.. 2.1	5
Bones	.. 0.9	0
Orbit	.. 0.7	0
Brain	.. 0.6	0
Miscellaneous	.. 2.2	30

Dew draws attention to the fact that seventy-six per cent for the liver is too high for cases in which the liver alone is involved, because in liver cases it is common to find other organs infected as well. And he says another error in figures of this nature is that owing to natural cure figures from hospital statistics probably place the infection rate in some organs too low. But as these factors will apply in any series of hydatid infections it seems that this table might be used for purposes of comparison with other records.

According to Mahadevan and Menon (1933) eight cases of hydatid disease have been recorded in the pathology department of the Madras Medical College. In this series four cysts were in the liver, two in the abdomen, one in the neck and one not known. The authors give particulars of seven cases of their own; three of these were in the liver, two in the peritoneal cavity, one in the kidney and one in the mammary gland. During the past five years four cases of hydatid have been seen in the Medical College, Calcutta; in two of these the liver only was infected, in one the liver, spleen and pelvis, and in the fourth the lung was the site of the cyst.

If the infection in which the liver, spleen and pelvis are counted as three we have twenty cysts to consider, and the liver is involved in ten, the abdomen (peritoneum) in five, cellular tissue (neck) in one, and the kidney, breast, spleen and lung in one each. These figures converted into percentages have been placed in a column beside D  v  's figures in the table. The five cases of abdominal hydatid have not been included in the table for Dew has excluded this type from D  v  's table also, because he says it is a common thing for cysts to be extruded unruptured from the liver into the peritoneal cavity where they acquire a fresh adventitious coat and may become attached to any of the organs covered by peritoneum, and it is therefore not possible to say whether they are

(Continued at foot of opposite page)

FURTHER NOTES ON PELLAGRA IN HYDERABAD DECCAN

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IN the *Indian Medical Gazette* of September 1931 the writer published an account of a series of cases of pellagra seen in the Leprosy Hospital, Dichpali, Hyderabad Deccan. The clinical manifestations were described as follows:— (a) dermatitis nearly always symmetrical, occurring most commonly on the back of the hands and the radial border of the forearms, and less commonly on other sites; (b) glossitis with excessive salivation; (c) nervous and mental symptoms sometimes culminating in suicide; and (d) gastro-intestinal symptoms (usually terminal). The mild cases showed only dermatitis and recovered; the moderately severe cases showed dermatitis and glossitis; and the severe cases showed nervous, mental and gastro-intestinal symptoms. The mortality rate was about 25 per cent. The causation of the disease was discussed but no definite opinion regarding causation was expressed. Of the cases reported in 1931 two more relapsed and died after the publication of the article. The other cases all cleared up but some had another attack a year later.

In the cold weather of 1931-32 a careful watch was kept for fresh manifestations of pellagra and 30 cases were seen. The first cases appeared in December 1931 and showed the typical dermatitis and glossitis, and the remaining cases were seen in January and February. We had a unique opportunity of watching the first signs of pellagra appear in

(Continued from previous page)

of primary origin. Dévé does not give a separate heading for the mammary gland so this case has not been included in the table either, but Dew states that the frequency of hydatid of the breast is 0.5 per cent.

At the first glance there appears to be a fairly close agreement between Dévé's figures and those from the Indian records, but Dévé's figures are calculated from 2,727 cysts and the Indian figures only represent twenty, so they are not comparable, and the fact that in such a small series as twenty cysts one each has been found in such comparatively uncommon sites as the breast, kidney, spleen and cellular tissue suggests the strong probability that the incidence of hydatid disease is commoner in India than the records in medical literature indicate.

REFERENCES

- Dew, H. R. (1928). *Hydatid Disease*. The Australasian Medical Publishing Company, Ltd., Sydney.
Mahadevan, V., and Menon, T. B. (1933). *Hydatid Disease in South India*. *Indian Med. Gaz.*, Vol. LXVIII. p. 206.

lepers, and we have also observed pellagra in non-leper patients. Until 1932 we never saw a case outside this institution, though we had three patients with the disease on admission. Our observations in 1932 have shown that the disease is not confined to this institution, nor is it confined to those suffering from leprosy. We have now seen one case in a leper convict in Hyderabad Central Jail, three cases in lepers in villages, and two cases in villagers otherwise healthy. We strongly suspect that the disease is not uncommon in the general population of Hyderabad. Our observations of the onset of the symptoms of pellagra have led us to the following conclusions.

Hyderabad has a dry cool season with marked differences between the day and night temperatures, and between sun and shade temperatures. This produces in many apparently-normal people a peculiar condition of the skin, particularly of the hands, arms, feet, and legs, in which perspiration is slight or absent and the skin dry, and there is a tendency to ichthyosis. The most exposed parts of the limbs are affected most. There is a marked tendency to keratosis and cracks in the soles of the feet, less commonly in the palms of the hands. The lips are often affected, and soreness and cracks are common. This appearance of the skin is apparently due to exposure to cold dry air and to the sun. It is seen in a high percentage of village people in the cold season and of course these signs are not those of pellagra, but it is particularly in the patient in whom this condition is marked that definite symptoms of pellagra are apt to develop. This tendency to dryness and cracks of the skin of the limbs and lips, if marked, perhaps indicates a tendency to pellagra.

In people suffering from nerve leprosy, there is an additional cause of this tendency in the fact that leprosy itself frequently causes anhydrosis, dryness and cracks of the skin of the limbs, and once again it is such patients who are prone to develop signs of pellagra.

Early signs.—The first definite signs of pellagra observed were in every case either definite patches of dermatitis on the hands and arms or else glossitis. In our first report of this disease we described dermatitis as always the first sign to appear. More careful observation has shown that this is not so, and that glossitis is sometimes seen first and may precede the dermatitis by several weeks.

The complaint of glossitis is typical. The people of Hyderabad are very fond of curries highly seasoned with chillies, and when glossitis develops the soreness of the tongue prevents them from eating such highly seasoned curries because of the marked burning sensation produced. Sometimes when this complaint is first made, there is very little visible change in the tongue, but after a short time the change becomes visible. The tongue is at first rather swollen and red. The dorsum of the tongue is

usually lightly coated and the margins of the tongue show a characteristic appearance with

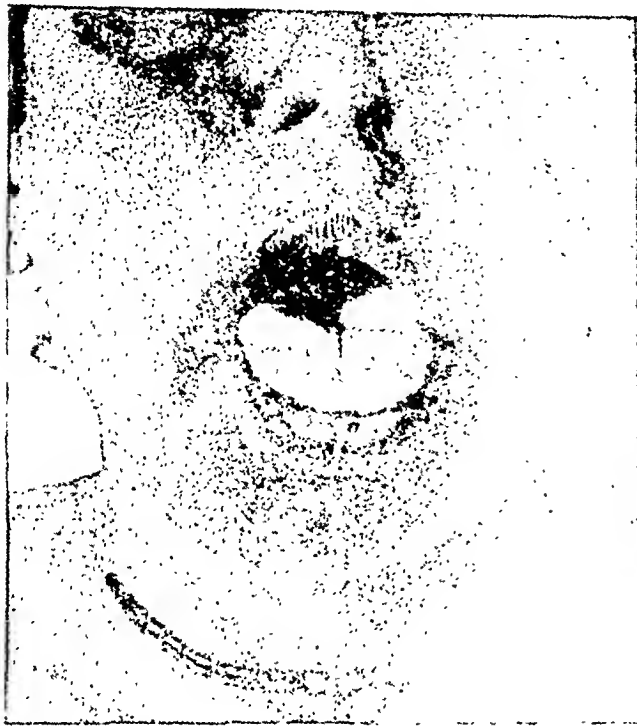


Fig. 1.—Pellagra—glossitis. Note swelling, enlarged papillae, and cracks of tongue; also blackening and desquamation of skin of lips and corners of mouth; excessive salivation (note saliva dropping from chin).

enlarged red papillae projecting above the surface. As glossitis progresses, in some cases cracks develop on the surface of the tongue which may present an appearance like syphilitic leucoplakia. With severe prolonged glossitis the tongue becomes denuded of epithelium and is small, atrophic and raw. The severer forms of glossitis are usually associated with inflammation and soreness of the lips, and of the mucous membrane of the mouth, pharynx and nasal passages. A typical case of severe glossitis with inflammation, cracks and blackening of the lips and the skin round the mouth, and with excessive salivation is seen in figure 1. The condition was associated with dermatitis and mental changes and later the patient died.

The distribution of the dermatitis we described carefully in our previous article. During 1932 we have been able to observe the early stages with greater accuracy. In most cases it starts as a small slightly-thickened erythematous patch on the skin on the dorsum of the hand between the bases of the thumb and the first finger. The erythema is transient, passing off in two or three days and leaving the epidermis thick, dry and a little blackened. This dark epidermis then cracks and desquamates in the centre, but the dermatitis tends to spread steadily over the dorsum of the hand (see figure 2) and up the radial border and back of the forearm. Unless the patient is seen



Fig. 2.—Hands of same patient as figure 1. Note symmetrical dermatitis with blackening and desquamation. This distribution of dermatitis is very typical.

in the first few days, the dermatitis on the hand may have nearly cleared up, and the forearms only may show dermatitis. The dermatitis rarely spreads above the elbow. Dermatitis usually appears first on the hand and arm, and in many of the slighter cases this may be the only sign present. Other cases show dermatitis on the dorsum of the feet and in other areas but here the patches are usually less defined. The association of dermatitis with exposure has been beautifully illustrated in some of our patients who wear sandals with a broad leather strap across the dorsum of the foot. In these patients the area covered by the strap was unaffected, the skin above and below showing dermatitis.

Recurrence.—Of seven patients who suffered from pellagra during the cold weather of 1930-31, and who recovered and were still under observation, two only relapsed during 1931-32.

Of thirty cases seen during 1931-32 in seven cases there was a history of similar attacks in previous years.

Treatment.—With the object of investigating the effect of treatment, the patients were divided into two batches, the one batch being treated and the other not. From humanitarian reasons however it was found advisable to give treatment to all the patients who showed at all marked signs of pellagra. Thus the value of the experiment was much diminished. All cases, both treated and untreated, recovered. In previous years the death rate was 25 per cent. In 1932 when all the more marked cases have been treated the death rate was nil; this appears to indicate that treatment is of considerable value, but the proof is incomplete for the cases seen during the last year have been on the whole of a less severe type than those seen in previous years. Whether the treatment prevented the development of severer forms is uncertain. We would therefore refrain from dogmatizing regarding the value of treatment for pellagra. The treatment given was based on that advocated by Goldberger. The ordinary diet, which consist of rice, *dāl* and *jawari*, was augmented by the addition of half a pound of meat a day. In addition powdered medicinal yeast 60 grains three times a day was given. Since all the cases were treated comparatively early and before the onset of severe gastro-intestinal symptoms, the treatment was tolerated well, but the severer cases seen in previous years would have been difficult or impossible to treat on these lines. In our experience early diagnosis is of vital importance as later on treatment by diet is extremely difficult, owing to gastro-intestinal symptoms making it impossible for the patient to take the prescribed diet.

Ætiology.—We can add little to our previous remarks about ætiology which is obscure.

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PELLAGRA IN GUNTUR*

By T. K. RAMAN, M.D., D.T.M. (Bengal)

(From the District Headquarters Hospital, Guntur)

As far as I am aware no definite case of pellagra has been reported in Madras Presidency although the disease has been reported from other parts of India. In 1931, Lowe reported 40 cases of pellagra occurring in the patients undergoing treatment for leprosy from Dichpali (Hyderabad).

During the course of my four years' stay in Guntur four cases of pellagra have come to my notice :—

Case 1.—A Hindu male, aged 30, was admitted to hospital in September 1930 for chronic dyspepsia. On investigation, he was found to be of unsound mind, showing symptoms of delirium and occasionally of mania. On further examination, he showed a symmetrical rash on the dorsum of both upper and lower extremities which according to him was only of three months' duration. The margins were circumscribed and scaly patches distributed all over, which could be easily removed leaving a depigmented area underneath. His mouth showed ulcerative stomatitis. No further investigation was possible as he refused to be kept in hospital.

Case 2 (figure 1).—A Hindu female, aged 35, was admitted in February 1931 for general weakness,



Fig. 1.

anæmia, and a rash over both the upper and lower extremities. The rash, according to the history, was of seven years' duration starting from the dorsum of both

(Continued from previous column)

Pellagra is associated with ill-balanced diet, but this may be merely a predisposing cause to an infection. Leprosy seems to have little to do with the causation of pellagra. In our experience it is less common in the severer forms of skin leprosy with marked widespread infiltration of the skin than in the slighter nerve forms of leprosy in which there is frequently anhydrosis of the extremities.

* A résumé, prepared by the Editor, of a paper read before the Third Andhra Provincial Medical Conference held at Guntur in April 1933.

the upper and lower extremities extending high up and becoming more and more thick and scaly. The patient was gradually getting weaker and on admission she had secondary anaemia, acute glossitis, diarrhoea, and occasional passage of mucus in the stools; under the microscope the stools showed undigested fat and polymorphonuclear leucocytes, evidence of damage to the mucous membrane of the intestine. The blood showed the picture of secondary anaemia.

The patient died of extreme weakness and anaemia.

A post-mortem examination was made; the more important findings are as follows:—*Heart and pericardium.* Heart, weight—10 ounces; the ragged surface of the pericardium showed evidence of pericarditis; there was also dilatation; the muscle showed fatty degeneration. *Liver,* weight—34 ounces; fatty mottled liver; *microscopically,* the normal structure of the liver is almost completely lost and replaced by fatty tissue with here and there a few surviving degenerate liver cells. *Spleen,* weight—5 ounces; infarction present; *microscopically,* slight thickening of the capsule, atrophy of the endothelial tissue, slight increase of the reticular fibres, atrophy of the lymphoid tissue. *Kidneys,* weight—4½ ounces each; infarction of the right kidney; *microscopically,* marked fatty degeneration of the tubular epithelium; shedding of the epithelium of the convoluted tubules. *Small intestines,* slight atrophy of the mucous membrane; no ulceration or cellular infiltration. *Large intestines,* marked atrophy of the mucous membrane. *Skin and subcutaneous tissue:*—On tracing the skin from the healthy to the affected side the noticeable feature is a marked atrophy of the epidermis in its entire depth; the superficial keratinized layers are being shed. No overgrowth of the Malpighian layer is seen, nor is there any sclerosis of the vessels.

Case 3 (figure 2).—A Hindu boy, aged 14, admitted in December 1932 for anaemia and skin disease. This is the second attack of the skin disease; the last one which occurred exactly one year ago lasted for only two months and completely disappeared. The condition has recurred again during the course of the last two weeks. The anaemia is getting worse and the patches are extending. On admission, he showed evidence of secondary anaemia with hæmic murmurs, and occasional attacks of diarrhoea. *Skin lesions:*—Patches typical of pellagra appearing on the dorsal aspects of both upper and lower extremities, extending as high as the elbow



Fig. 2.

and the knee respectively. On investigating the diet, we found that he took rice—three ounces—three times a day, brinjals, cucumber and mutton once a week, eggs once a week, and dāl and maize occasionally. He eats no rice on the day he eats maize; he takes no milk, but takes butter-milk daily.

He was put on liver extract—8 ounces—daily, toddy, 6 ounces, and bread and milk. The symptoms gradually disappeared a month after admission.

Case 4 (figure 3).—A Mohammedan male, aged 20 years, a tailor by occupation, was admitted on 9th



Fig. 3.—Note the patch on the right side of the neck.

March, 1933. He came with a complaint of indigestion, loss of appetite, and soreness of the mouth and tongue. On investigation it was found that this was the second attack. The first attack was one year ago during the same season of the year. He had slight oedema of the legs, and skin lesions, typical of pellagra, on both hands and legs, and on both sides of the neck behind. The symptoms had disappeared in the course of a month by discarding rice diet and taking only milk, bread and fruits. The present attack appeared about two months ago. There was no oedema. Indigestion and loss of appetite were present from the onset. The lesion appeared first on the dorsum of both the hands and spread up to the elbow. A few days later symptoms appeared on the dorsum of the feet. The lesions on the neck appeared along with that of the hands. The patches are dark and scaly, can be peeled off from the skin and the outer margin of the patch is quite distinct, a characteristic which distinguishes it from ichthyosis which it closely simulates. He is a fairly well-nourished boy, very slightly anaemic; occasionally he gets attacks of stomatitis. The knee jerks are sluggish. On investigating the diet we found that he eats milled rice—four ounces—three times a day, meat once a week, vegetables—two ounces—daily, dāl, fish, butter-milk, and ghee, occasionally; he takes no milk and never eats maize. The patient was put on toddy, eight ounces a day, iron, arsenic and strychnine by mouth. The patches had completely disappeared by 27th March, 1933, but the symptoms started again on 31st March, 1933. A red hyperæmic patch appeared on the dorsum of the right hand and the right side of the neck. On 3rd April, 1933, the red induration had

turned to a dark, coppery-red colour. Next day it became darker, and three days later scaly patches appeared. In this case one was able to follow the course of the pellagra from the red congested area to the final stage of dark scaly patches with circumscribed areas.

Discussion

During the course of investigation of beri-beri in this district, I was surprised not to find any pellagra, a disease closely simulating beri-beri in its aetiology; both are vitamin-deficiency diseases. Although I was on the lookout for the disease I was only able to spot the four cases mentioned above, during the course of the last four years. The last case was accidentally spotted by me in the out-patient department, being treated as a case of indigestion and a condition of the skin. No doubt can exist as to diagnosis of the four cases described above. Case 1 illustrates the nervous complications arising in the course of pellagra. Case 2 has given us the full opportunity of studying the pathology and morbid anatomy of the disease. From cases 3 and 4, one was able to study the clinical aspect of the disease and the effect of vitamin B administration. Case 4 cannot be fully explained; the administration of the pellagra-preventing factor, though it produced rapid amelioration of symptoms, did not prevent the recurrence of the disease. In this case, evidence is produced against the theory that maize is the causative agent in the production of pellagra, since the patient has never taken maize at any time.

My thanks to Dr. T. Bhaskara Menon, M.D., M.R.C.P. (London), for the microscopic examination of the specimens.

REFERENCE

Lowe, J. (1931). *Indian Med. Gaz.*, Vol. LXVI, p. 491.

ON THE INCIDENCE OF ARSENICAL DERMATITIS*

By H. K. CHAKRAVARTY, L.M.P.

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THE report covers a period of six years from 1927 to 1932, during which the total number of injections made was 3,914; during this period there were 15 cases of exfoliative dermatitis that could be attributed to arsenic injections. Novarsenobillon, sulfarsenol and thiosarmine were used; the number of cases treated with novarsenobillon was 449, with sulfarsenol 74, and with thiosarmine 50, and the respective number of injections given of each was 3,530, 468, and 600.

It is interesting to note that dermatitis occurred only in cases treated with the first-named drug.

From the above it will be seen that the cases in which the dermatitis occurred were few and

far between. If the incidence of dermatitis be so rare in hospital practice it must be more rare in private practice and there may be instances in which a general practitioner hardly comes across a case of arsenical dermatitis in his practice. It will, therefore, be worth while describing briefly the chief characters of the cutaneous affections that may occur under arsenical treatment.

Urticaria is common; it may appear during or immediately after injection, but generally disappears within a few hours. Some patients complain of itching of some particular part of the body after each injection and this itching may be a symptom of intolerance. In some cases after a number of injections have been made erythema may appear, the rash of which sometimes remains patchy and resembles seborrhoeic eczema. Hyperkeratosis of the palmar and plantar surfaces and atrophy of the nails, toxic alopecia of the areata type, herpes zoster due to inflammation of posterior root ganglia, and herpes simplex involving the vulva and lips, will occasionally occur. Acne-vulgaris boils and carbuncles are aggravated by arsenic or may appear for the first time under the influence of the drug, and there is occasionally a focal reaction at the site of an old chancre.

The most distressing condition, however, is exfoliative dermatitis. The eruptions appear on the inner aspect of the arms, forearms, thighs, lower part of abdomen, as well as on the face, and in bad cases may extend over the whole body within 72 hours. The first appearance is like a measles rash with severe itching, which is at first limited to certain areas but rapidly extends all over the body, becomes confluent, and in a few days forms into vesicles and pustules. The whole body is swollen, the face oedematous and disfigured, the eyes cannot be opened and there may be conjunctivitis. This first stage is called the dry stage. In this stage there is intense itching all over the body. There is a rise of temperature, usually throughout the disease, both in the dry and the weeping stages. After a week or so the weeping stage begins when the vesicles and pustules are ruptured and discharging ulcers are formed. In the worst cases the cuticle comes off like a glove from the hands and feet. There is severe burning pain all over the body, and the patients want to dip the whole body into water. After the separation of the cuticle, the cutis vera is exposed and in places ulcers form and extend deep down to the muscle. Septic complications may start, leading to multiple boils all over the body, or cellulitis. The patient often becomes extremely prostrated, bed-sores form, and toxæmia, broncho-pneumonia or intestinal hæmorrhage are not uncommon terminal conditions.

Recovery is always slow and convalescence protracted. One peculiarity of arsenic poisoning is that if one organ is involved to a serious extent, the other vital organs are generally

* Rearranged by Editor.

spared. In extensive exfoliative dermatitis, the liver and kidneys may be spared, and in cases in which the liver is badly involved, the kidneys and heart may escape altogether.

The following table gives the incidence of dermatitis, year by year.

NOVARSENOBILLON					SULFARSENOL AND THIOSARMIN		
Year	Number of cases	Number of injections	Incidence of dermatitis	Percentage of dermatitis	Number of cases	Number of injections	Incidence of dermatitis
1927	104	770	4	3.84	2	24	Nil
1928	103	824	4	3.88	6	48	"
1929	90	720	2	2.22	12	72	"
1930	65	520	3	4.61	10	60	"
1931	62	496	2	3.23	30	180	"
1932	25	200	Nil	Nil	64	684	"
TOTAL	449	3,530	15	..	124	1,068	Nil

The following table gives the time of appearance of the dermatitis in relation to the number of doses and the total dose of the arsenical given.

Number of cases	Number of injections prior to onset	Total dose prior to onset in grammes
1	1	0.3
6	3	0.9
6	4	1.2
1	6	2.1
1	7	2.55

All our patients being women they get the first four injections of 0.3 gm. each and the next four injections of 0.45 gm. each, making a total of 3 grammes. They also get a course of bismuth or mercury injections along with the arsenic treatment.

From the above it is evident that the arsenical dermatitis may be due to natural hypersensitiveness to arsenic, as in one of these cases it occurred after one injection only. Undoubtedly in the majority of cases the skin lesions are due to the cumulative toxic effects and these are due to injury to the important organs concerned, namely the liver and kidneys, by the chronic pathological changes caused by the *Spirochæta pallida* in some cases, by bacterial or other diseases in others, and by the administration of mercury in probably not a few. In two cases of our series in which mercury (4 c.cm. of mercurisol) was injected along with the arsenic, a very severe form of dermatitis appeared after the injection; both of these patients had albuminuria.

On the night before the injection the patients were given a light diet, they were allowed no food in the morning prior to the injection and for the rest of the day they were given only

barley water and milk. A dose of glucose was given with alkali an hour before the injection to protect the liver cells. A saline purge was given the previous night and again on the following morning to help excretion of arsenic. Patients were kept in bed on the day of the

injection. In cases of accidental extravasation of novarsenobillon solution into the subcutaneous tissues, we have got very good results by immediately injecting sodium thiosulphate solution subcutaneously in the infiltrated zone. This immediately lessens the local irritation, the patient is relieved of the extreme pain, and after-effects are obviated.

In 1932 at the suggestion of Lieut.-Colonel Denham-White, 3 c.cm. of 10 per cent. sodium thiosulphate solution was injected after the fourth dose of novarsenobillon in 25 cases; in none of these cases has dermatitis occurred.

Treatment for dermatitis.—The usual treatment was followed; patients were put to bed and kept at absolute rest; liquid carbohydrate diet, such as barley water and glucose, and milk were given; protein and fat were restricted; calamine lotion was applied externally in the dry stage to allay itching; an alkaline mixture containing potassium citrate, potassium bicarbonate, and urotropine was given orally several times a day; saline purgatives were given daily to help the excretion of the arsenic; ichthyol, grains ii, in pill form, was given twice a day; and 10 per cent sodium thiosulphate solution was given intravenously or intramuscularly every alternate day or every day up to 4 c.cm. at a time, for five or six injections, or until the progress of the disease was checked. In the weeping stage ichthyol in arachis oil was applied externally over the cracked and painful areas. In prostrated conditions stimulants were administered, the patient was protected from cold, and the ulcers kept clean. After recovery no further arsenic treatment was given for at least a year.

Some illustrating case notes are appended below :—

(1) K., Hindu female, aged 30 years, admitted on 27th October, 1930. Wassermann reaction strongly positive. She was treated with novarsenobillon and

mercurosol, alternately. After the third injection the reactionary fever had persisted for three days, instead of subsiding within 24 hours as usually happens. When the next dose of one c.cm. mercurosol was injected the temperature rose again for one day. This temperature started with a rigor and was thought to be malaria, but no parasites were detected on blood examination. Two weeks after the third injection the fourth dose of novarsenobillon was given intravenously; two days later an itching erythematous rash appeared on the chest and thighs, there was swelling of the face, and pain all over the body. After ten days pustules started to develop at the roots of hairs and there was a slight rise of temperature. The skin began to scale off leaving discharging ulcers.

The dermatitis persisted for one month during which time five injections of thiosulphate were given. The itching sensation continued for a month more.

(2) S., Hindu female, aged 23 years, admitted on 12th June, 1931. Wassermann reaction strongly positive. She was treated with novarsenobillon and bismostab, given alternately. Seven days after the third injection of novarsenobillon (0.3 gramme) she developed intense itching; sodium thiosulphate was immediately injected intravenously. The itching disappeared and novarsenobillon was resumed after two weeks, but each injection was preceded by an injection of sodium thiosulphate. Bismostab was also continued. She had five more injections of novarsenobillon, one of 0.3 gramme and four of 0.45 gramme, each preceded by sodium thiosulphate; she developed no further symptoms of intolerance. She was discharged cured on 4th October, 1931, with Wassermann reaction negative.

(3) G., Hindu female, aged 25 years, admitted on 9th March, 1931. Wassermann reaction negative at first, but after a provocative injection of novarsenobillon of 0.3 gramme it was moderately positive. She was then treated with novarsenobillon and mercurosol, 1 c.cm., alternately. She was given four injections of 0.3 gramme novarsenobillon and one of 0.45 gramme. After the fifth injection of novarsenobillon she continued to have a daily rise of temperature; this ranged from 100° to 103°F. On the third day dermatitis appeared over the face, axillæ, forearms and thighs. The urine was free from albumen, though scanty in amount; the motions were loose. Her face was swollen so much that she could not open her eyes, and she had conjunctivitis. Her skin came off in flakes leaving profusely discharging ulcers. She then developed multiple boils all over the body, bed-sores on her back, buttock, and heels, and her condition was precarious.

The usual treatment was given; she received six injections of sodium thiosulphate of 2 c.cm. each, intramuscularly, as the bend of the elbow was involved in dermatitis intravenous injection was not possible. Her condition became very bad and she was given brandy, digitalis, and strychnine. She recovered, and was discharged cured after eight weeks.

A PLEA FOR COLLAPSE THERAPY IN THE EARLY STAGES OF PULMONARY TUBERCULOSIS*

By P. T. PATEL, M.D. (Lond.), M.R.C.P. (Lond.),
B.T.M. & H. (Cantab.), F.C.P.S. (Bom.)

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THE medical profession in this country has been slow to take advantage of one of the most important recent advances in the treatment of

pulmonary tuberculosis. Doctors are liable to rely too much on remedies such as creosote, cod-liver oil, calcium and the various gold preparations, and, without considering sufficiently the economic aspect, to advise their patients to go away for a change of air or to a sanatorium. The fundamental measure in the treatment of tuberculosis should be rest of the affected part; other methods can then be employed to raise the resistance of the body as a whole against the infection. The only way that the lung can be given rest is by causing collapse of the whole or part of the lung. The best results are obtained in early cases of tuberculosis, and therefore our aim should be the early diagnosis of the lesions and the adoption of collapse therapy without delay.

The methods by which this form of treatment can be applied are artificial pneumothorax, phrenicotomy and phrenic evulsion, apicolysis (i.e., paraffin compression), and thoracoplasty. Of these the first mentioned is the simplest and can be performed by the average practitioner in any hospital or dispensary.

Phrenic evulsion is also a simple operation and can be undertaken under a local anæsthetic; it is very often a useful adjunct to the pneumothorax treatment, especially in cases in which there are basal lesions with adhesions, but it is also adopted as an independent form of treatment. Phrenic evulsion causes paralysis of the diaphragm on one side, with the subsequent limiting of the movements of the lung.

Apicolysis, the name given to the operation of injecting paraffin to cause collapse of the apex of the lung, and thoracoplasty are both more formidable operations which should only be undertaken by experienced surgeons in well-equipped hospitals.

Indications for artificial pneumothorax.—It has been said that pneumothorax therapy is not necessary in early cases when the disease is still curable by sanatorium and other methods of treatment, but the condition is seldom diagnosed at this stage in this country. On the other hand no case is too advanced, provided it is one-sided and there are no adhesions which would prevent the compression of the lung. The essential factor is the softness of the lung which can be judged by clinical and x-ray examinations. There is no reason why a bilateral operation should not be done as long as there is healthy lung tissue sufficient for respiratory exchange.

Any early active case of pulmonary tuberculosis, either with one or both lungs affected, is suitable for this line of treatment. The persistence of any of the following symptoms and signs is an indication of 'activity':—rise of temperature, hæmoptysis, loss of weight, tubercle bacilli in the sputum, toxæmia, general failing of health and persistent catarrhal signs in the lungs, and persistent pleural effusion. In

* A résumé, prepared by the Editor, of a paper read before the Medical Research Section of the Indian Science Congress, Bangalore, 1932.

the last instance gas replacement after aspiration of fluid is very successful.

Ambulatory pneumothorax.—Patients who are not seriously ill can be treated even as out-patients and after the injection can be sent home to return at stated intervals for refills. Of course they must stay in bed at the beginning, and have fresh air, a good nourishing diet, and tonics. We have many cases taking treatment like this after the first injection and getting on well.

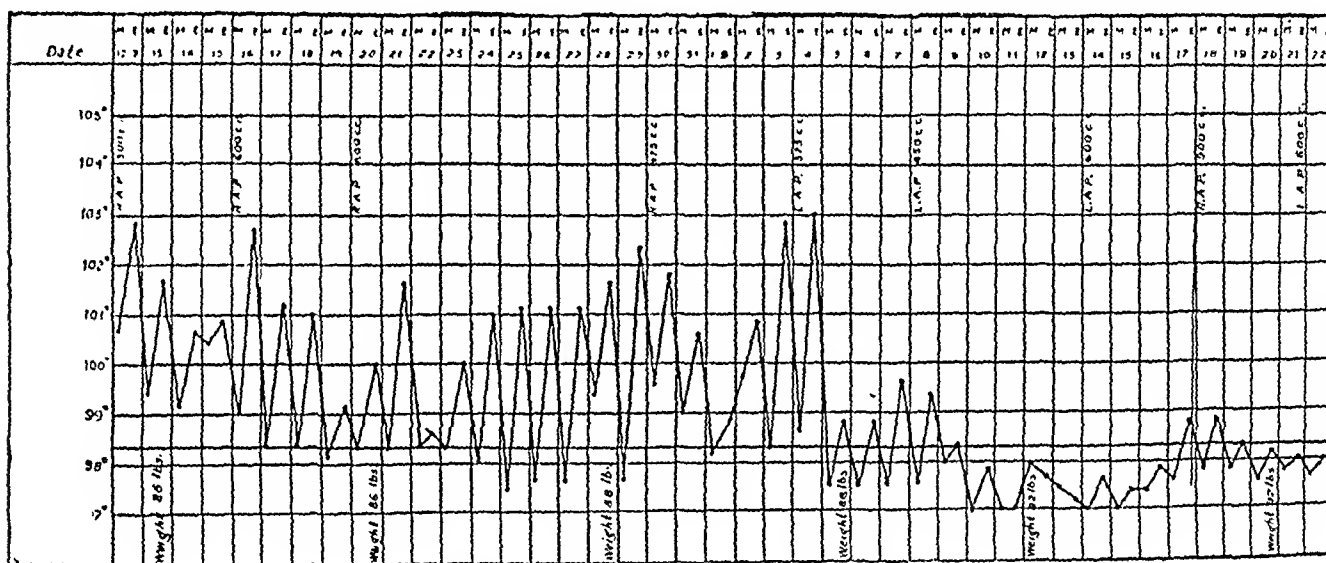
The contraindications are extensive bilateral disease with cavitation, chronic fibroid disease, tuberculous enteritis, asthma, and severe constitutional disturbances.

Apparatus.—An elaborate apparatus is unnecessary, and one can be improvised on the simple principle of replacement of air by water

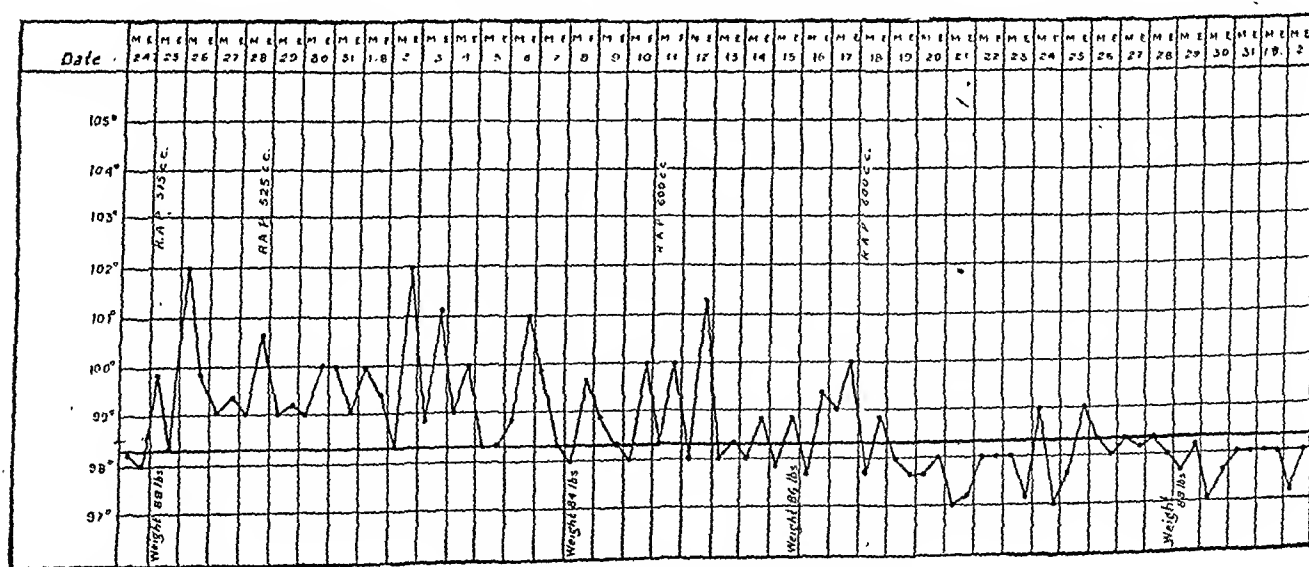
As regards technique of the operation, the amount of gas to be filled in and the intervals to be observed, I would refer the reader to my article in the *Indian Medical Gazette* of December 1927.* A practical acquaintance with all the details is, however, very necessary, and can only be obtained by attending the hospitals and clinics where this therapy is practised.

Illustrative cases

A bilateral case.—The patient, a man, aged 20, was admitted on 12th July for evening rise of temperature, cough with expectoration, and loss of weight. Clinical and x-ray examination showed signs in both the lungs, and sputum showed tubercle bacilli. Artificial pneumothorax was started first on the right side, and then on the left side. His temperature came under control after about a month's treatment and remained normal till he was discharged. He showed definite increase in weight by 14 pounds, and improved in all respects. He



Temperature chart in the bilateral case.



Temperature chart in the unilateral case.

from one bottle to another; to avoid the water manometer which is troublesome and unnecessarily increases the size of the apparatus, a portable apparatus with an aneroid manometer, like that made by Bullitte of Paris for Professor Mainini, is most suitable and cheap.

is taking ambulatory treatment now. He had a bad fistula in ano which also is healing up after operation.

*The reader is also referred to our Current Topics section. We have here reproduced a chapter on this subject from a recently-published book.

Unilateral case.—The patient, a woman, aged 28, was admitted on 24th July for evening rise of temperature, loss of weight, and cough with purulent expectoration. Clinical and x-ray examination showed signs of tuberculosis in the right side of the chest; tubercle bacilli were found in the sputum. Weight on admission was 88 pounds. Artificial pneumothorax was performed on the right side. The temperature came down after 25 days, and remained normal until she was discharged. There was definite increase in weight to 90 pounds. Symptoms were much relieved. The patient is still under treatment. Further details can be seen from the table and the temperature chart.

A table showing the amounts of air injected and the pressure before and after the injection and a temperature chart for each of these cases are given.

RIGHT SIDE

ARTIFICIAL PNEUMOTHORAX

Date	Pressure before	Air injected in cubic centimetres	Pressure after
12-6-32	— 5, —15	300	— 6, — 3
16-6-32	— 5, —15	600	— 6, — 3
21-6-32	— 5, —15	600	—10, — 5
30-6-32	— 5, —10	975	— 8, — 5
18-7-32	— 4, —10	900	— 7, — 4
29-7-32	—10, — 5	875	— 0, — 7
18-8-32	—10, — 5	975	— 2, — 5
2-9-32	—10, — 5	1,125	— 5, + 1
18-9-32	— 8, — 5	1,050	— 3, — 1
4-10-32	— 7, — 4	1,200	— 3, + 2
23-10-32	— 0, — 5	1,175	— 0, + 5

LEFT SIDE

ARTIFICIAL PNEUMOTHORAX

Date	Pressure before	Air injected in cubic centimetres	Pressure after
3-7-32	— 5, —15	375	—10, — 5
7-7-32	— 5, —15	450	—10, — 5
13-7-32	— 5, —10	600	— 8, — 4
21-7-32	— 4, — 7	600	— 5, — 0
3-8-32	— 8, — 5	750	— 5, + 2
30-8-32	— 8, — 1	675	— 6, — 1
8-9-32	—10, — 5	675	— 6, — 1
22-9-32	—10, — 4	900	— 6, + 1
11-10-32	—10, — 5	750	— 5, + 1
2-11-32	— 5, —10	975	+ 2, — 8

Mrs. Z.

RIGHT ARTIFICIAL PNEUMOTHORAX

Date	Pressure before	Air injected in cubic centimetres	Pressure after
25-7-32	— 5, —10	375	—10, — 0
29-7-32	—10, — 5	525	— 5, — 0
4-8-32	—10, — 5	600	— 2, + 2
10-8-32	—10, — 5	600	+ 3, + 5
18-8-32	—10, — 5	525	— 3, + 1
26-8-32	—10, — 5	525	— 3, + 3
2-9-32	— 8, — 5	750	— 0, + 3
13-9-32	— 5, — 1	575	— 1, + 3
22-9-32	—10, — 5	675	0, + 3
30-9-32	—10, — 3	615	0, + 3
18-10-32	— 5, —10	675	0, + 3

The collapse therapy can be carried out in any climate provided the patient is under constant observation and takes ordinary measures of rest, open air, sufficient nourishment, etc. Climate by itself has no special influence in the cure of pulmonary tuberculosis compared to the early control by collapse therapy, and from experience of cases treated in Bombay for some years I quite agree with Knoff (1931) that there is no specific climate for tuberculosis; if I had to choose between having a patient under special medical supervision with mental and physical rest in his home climate, or sending him even to an 'ideal' climate where he would merely do as he pleased, I would prefer the former, believing he would have a better chance for recovery.

Results

Unilateral cases.—Out of the 25 cases that have come under my treatment during the last two years, 19 cases are practically cured; x-ray examinations and physical signs and absence of tubercle bacilli indicate that the lesions are healed, no tubercle bacilli can be found in their sputum, and they are mostly following their normal vocations.

Bilateral cases.—The results here are not so successful, but eight out of twelve patients have improved to the extent indicated above.

REFERENCES

- Burrell, L. S. T. (1929). *Recent Advances in Pulmonary Tuberculosis*. London: J. & A. Churchill.
 Knoff, S. A. (1931). *Journ. Amer. Med. Assoc.*, Vol. XCVI, p. 2023.
 Patel, P. T. (1927). *Indian Med. Gaz.*, Vol. LXII, p. 682.
 Patel, P. T. (1929). *Infectious Diseases and other Fevers in India*. Calcutta: Butterworth & Co.
 Riviere, C. (1927). *Pneumothorax and Surgical Treatment of Pulmonary Tuberculosis*. London: Humphrey Milford, Oxford University Press.

A FEW OBSERVATIONS ON THE PHARMACOLOGY AND THERAPEUTICS OF MUSCLE EXTRACT

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MUSCLE extract has for some time been used in the skin department of the Calcutta School of Tropical Medicine in the treatment of certain skin diseases, and Lieut.-Colonel H. W. Acton, the director of the school, was kind enough to supply me with muscle extract made in the chemical department of the school. A few cases of grave vascular and kidney diseases were treated with this muscle extract and the results were so striking that it encouraged me to proceed with further investigation of its action in other cases.

Preparation of the muscle extract

Bullock's heart muscle was used for the preparation of the extract as recommended by

Drury and Szent-Györgyi (1929). The heart muscle was finely minced and then treated with 5 per cent trichlor-acetic acid in proportion of 1 c.cm. of the dilute acid to 1 gramme of the muscle and allowed to stand overnight. The fluid was pressed out and filtered. The filtrate was then neutralized.

When larger quantities of muscle extract had to be prepared, the muscle was treated with 1 per cent solution of trichlor-acetic acid and kept for half an hour with occasional stirring; the mixture was then heated up to 90°C. and subsequently cooled. The fluid was pressed out, filtered, neutralized, and standardized.

My thanks are due to Mr. A. C. Roy, who actually prepared the muscle extract, for the short description of the method of preparation that has been given above.

The hydrogen-ion concentration of the muscle extract after neutralization should be slightly on the acid side, viz, pH 6.8 to 6.9. The slight acidity causes intense swelling and pain, when the drug is injected subcutaneously. It should always be injected intramuscularly, so as to make it potent by de-amination in contact with muscle tissues, resulting in the formation of ammonia therein, which may be one of the factors in imparting the sensation of well-being which the patients usually experience after muscle extract is given.

Thrombo-angitis obliterans

The practical application of muscle extract as a vaso-dilator was recorded by Schwartzmann (1931) who used it in thrombo-angitis obliterans and allied conditions, with satisfactory results.

Two cases of thrombo-angitis obliterans were treated in the wards of the Medical College Hospital. One of them was a child who arrived too late, but the other was treated successfully with muscle extract.

Case 1.—Hindu male child, aged 1 year, was admitted on 18th May, 1932, for treatment of thrombo-angitis obliterans and gangrene of the toes. This case was complicated with ileus. The patient arrived too late, as only two doses of muscle extract could be given, and the child died of ileus on the third day after admission.

Case 2.—Hindu male, aged 22 years, was admitted for treatment of fever of 6 days' duration, temperature on admission being 104°F. On examination, bronchopneumonic patches were found in the lungs. His urine contained a large quantity of albumen and gave a positive reaction with dimethyl-para-amino-benzaldehyde solution. The case was diagnosed as influenza. The fever came down to normal on 27th June, but on the same evening a swelling of the lower third of his left leg was observed which quickly extended to the thigh within a day. On examination no pulsation could be felt over his dorsalis pedis and posterior tibial arteries. The left toes were cold. The Wassermann reaction of his serum was negative. Injection of muscle extract was commenced on 28th June. On 30th June, the swelling of the leg went down but some dark ischæmic spots appeared on the left foot and leg, the most marked being on the dorsum of the left half of the left little toe and a big patch, 1½ inches by 1 inch, on the postero-lateral aspect of the left knee; these

patches became hyperæsthetic. A feeble pulsation of the dorsalis pedis artery gradually returned. The patient received 20 injections of muscle extract up to 27th July, in 1 c.cm. doses. Some of the patches, which turned black, gradually disappeared, but three patches on the inner aspect of the knee joint became ulcerated after a period of burning sensation. On 3rd August, a third course of muscle extract was begun as the ulcers remained dormant and showed no signs of healing. These ulcers then quickly granulated and healed up. The patient was discharged cured on 28th September.

Arterio-sclerosis

Schwartzmann (1931) reported satisfactory results in fourteen cases of intermittent claudication due to arterio-sclerosis. Two cases of advanced arterio-sclerosis were treated with muscle extract in my wards, but the results were not satisfactory.

It is difficult to understand how the muscle extract could have any beneficial effect on advanced cases with calcified atheromatous arteries. In both my cases, the muscle extract produced embarrassment of the overloaded heart. In early cases, however, muscle extract may produce a beneficial effect by relaxation of the spasm of the vasa vasorum of the affected arteries.

Angina pectoris

The vaso-dilator action of the muscle extract was suggested by its beneficial action in relieving distress and pain in angina pectoris. Schwartzmann (1931) recorded wonderful results in 9 out of 11 cases with a history of coronary thrombosis and myocardial disease. The action is attributed to vaso-dilator action by overcoming the vascular spasm in that disease. The spasm is supposed to be due to the effect of pressor substances generated in excess or to the balance of pressor or depressor substances being upset. The pain is due to ischæmia of the heart muscle which is relieved by vaso-dilatation. In case 2, reported above, the pain and hyperæsthesia was due to the ischæmic condition of the patches of skin involved.

Nephro-sclerosis

Muscle extract exerts fibrolytic action in pathological fibrosis of internal organs. It cannot be expected that it should have any such action on physiological scar tissues. Acton used this substance as a fibrolytic agent in the treatment of elephantiasis, scleroderma, etc., in the School of Tropical Medicine. In many cases of elephantiasis remarkable diminution in the size of the affected limbs was noted. The fibrolytic action is probably due to the increased blood supply of the affected organs and to the increased number of phagocytic leucocytes coming in contact with fibrous connective tissues. This action of the muscle extract has been utilized in the treatment of nephro-sclerosis, mitral stenosis, cirrhosis of the liver and various other diseases associated with fibrosis

in my wards. The following are some of the illustrative cases:—

Case 3.—Hindu female, aged 17 years, was admitted on 10th November, 1931, with signs of general anasarca and fever of 5 months' duration. Physical examination revealed enlarged liver, tenderness in the right iliac region, and slight tachycardia. The urine was scanty and showed on examination copious albumen (0.4 per cent), hyaline and granular casts, and a few red blood cells.

She was put on Epstein's diet and urea. There followed an increase in the quantity of urine and diminution of oedema all over. The fever was found to be due to malaria (*Plasmodium malaric*) and was checked by atebirin. The biochemical examinations now showed the following results:—Blood cholesterol 0.01 per cent, blood chloride 0.544 per cent, blood urea 0.028 per cent, blood non-protein nitrogen 0.056 per cent, and urinary albumin 0.2 per cent. The urea-concentration test showed defective elimination of urea, viz. 0.5 per cent in the third sample passed two hours after the dose of urea. There was, however, no further improvement for some time. The intramuscular injections of muscle extract were commenced from 10th January, 1932. After seven daily injections of muscle extract, the elimination of nitrogenous metabolic products increased and the urea-concentration test showed excretion of 1.2 per cent of urea in the third sample passed two hours after the load of urea. There was however no further improvement, although seven more injections of muscle extract were given. The search for septic foci revealed salpingitis of the left side, for which the patient was treated with injections of milk. Each injection of milk was followed by transient reappearance of oedema and this was attributed to transient exacerbation of nephrosis due to increased elimination of toxins from the septic foci. During this time excretion of urea in the urea-concentration tests fluctuated between 0.9 and 1.2 per cent. The infected tonsils were then removed. A further exhibition of muscle extract increased the elimination of urea to 1.5 per cent after which it remained stationary. The patient still suffered from recurring temporary exacerbation of chronic nephrosis. When the patient was discharged on 25th May, she was free from oedema, but the elimination of urea was only 1.5 per cent.

This patient was suffering from chronic nephrosis, with secondary nephro-sclerosis. The toxin from the septic foci was keeping up chronic nephrosis. The removal of septic foci ameliorated her condition, but left the renal tubules in an allergic state; this allowed an exacerbation of the nephrosis on the slightest provocation. The fibrolytic action of the muscle extract was responsible for increased elimination of nitrogenous metabolic products.

Case 4.—Hindu male, aged 26 years, was admitted on 5th April for treatment of ascites and general anasarca of two and a half years' duration. The case was diagnosed as chronic nephrosis with secondary nephro-sclerosis. The urea-concentration test showed elimination of 1.3 per cent urea in the third sample. The dye test showed 35 per cent elimination in two hours. He was anæmic, his blood count showing 3,210,000 red blood cells, and 5,616 white blood cells per cubic millimetre, and hæmoglobin 60 per cent. Treatment with muscle extract was begun on 13th August, and ten injections were finished on 27th August. The urea-concentration test showed 1.6 per cent of urea on 27th August. Euphyllin was given twice daily *per os*. The patient's condition went on improving. When he was discharged on 5th September, he was free from oedema and ascites and showed normal elimination of urea.

Case 5.—Hindu female, aged 36 years, complained of intense headache for 6 months, which was thought to

be neuralgic. Her blood pressure was high; systolic pressure was 160 mm. Hg. and diastolic 100 mm. Her elimination of urea was 1.6 two hours after the load of urea was given. Ten injections of muscle extract increased the elimination of urea to 2 per cent and reduced the systolic and diastolic pressures to 120 and 90 mm. Hg., respectively, but the headache remained the same as before.

Case 6.—Hindu male, aged 60 years, was admitted on 17th August, for treatment of oedema of the lower extremities, scrotum, abdomen and hands, of 8 months' duration. His urine contained 0.08 per cent albumen. The urea-concentration test showed elimination of urea only 1.15 per cent in the third sample drawn two hours after the urea load. Blood urea was 0.05 per cent.

Treatment with muscle extract was commenced from 23rd August, but it had to be stopped as the patient got an attack of influenza on 26th August. His temperature rose up to 103° and came down to normal on 30th August. Five more injections of muscle extract were given from 1st to 5th November. He was getting alkaline mixture all this time. When the patient was discharged on 13th September his urine was free from albumen, his elimination of urea was normal, his blood urea was 0.18 per cent and total non-protein nitrogen 0.28 per cent.

High blood pressure

It was seen in case 5, that along with the restoration of the normal functions of the kidneys, there was certain amount of reduction of high systolic and diastolic blood pressure. In the following two cases of high blood pressure the exhibition of muscle extract gave different results. In one case, the ætiological factor was the same as that of case 5, but in the other it was due to dysfunction of the endocrine system. The lowering of the high blood pressure in the latter case by muscle extract was due to relieving the chronic spasm of the peripheral arterioles which developed as a result of reaction to toxic bases or pressor endocrine substances circulating in the blood.

Case 7.—Hindu male, aged 45 years, was admitted on 18th February for treatment of high blood pressure. His principal complaints were giddiness and sleeplessness for over a month, pain in the thigh for four years, scanty urine and constipation. He had fever 8 years ago and swelling of the knee joints which started four years ago and kept on recurring at frequent intervals. The patient was very weak and suffered from pyorrhœa alveolaris. His systolic and diastolic pressures were 215 and 115 mm. Hg. respectively. His urine contained albumen and showed a few granular casts and pus cells. His blood urea was 0.06 per cent, non-protein nitrogen 0.977 per cent and cholesterol 256 mgm. per cent. The Wassermann reaction was negative. The urea-concentration test showed elimination of urea to be 1.6 per cent in the third sample.

After eight daily injections of muscle extract in 0.5 c.c.m. doses, all the complaints showed signs of amelioration; his systolic blood pressure came down to 135 mm. Hg. Biochemical findings of the blood were as follows:—Blood urea 0.04 per cent, non-protein nitrogen 0.056 per cent, cholesterol 130 mgm. per cent, and phosphate 0.0012 per cent. The muscle extract had to be discontinued owing to failure of supply, during which the systolic blood pressure rose to 170 mm. Hg., but again went down on resuming the treatment with muscle extract. He got 30 injections altogether after which his condition returned to normal; his urine became free from albumen; on 29th March his urea-concentration test showed normal elimination of urea; and his systolic and diastolic blood pressures were 130 and 75 mm. Hg. respectively. The patient left the hospital on 1st April free from all complaints.

It appears that the high blood pressure disappeared in this case with the removal of its cause, *viz.* nephro-sclerosis. In the following case of hyperpiesia with intermittent claudication and in which the kidneys were normally functioning, the muscle extract exerted only a temporary effect.

Case 8.—Hindu male, aged 36 years, was admitted on 26th May for treatment of hemiplegia. The patient gave a history of a sudden attack of unconsciousness for a few hours; on regaining consciousness he found that both the extremities of his left side were paralysed. On admission, his systolic and diastolic blood pressures were found to be 195 and 100 mm. Hg. respectively. His urine did not show any abnormal constituent. The urea-concentration test showed normal elimination of urea. The radial and other palpable arteries were soft and elastic, and no arterio-sclerotic changes were found in the retina. The case was diagnosed as hyperpiesia. Lumbar puncture showed a normal cerebrospinal fluid. The hemiplegia was attributed to intermittent claudication of a branch of the right lenticulostriate artery.

The injection of muscle extract was commenced on 2nd June. Hemiplegia disappeared quickly, and his systolic blood pressure went down to 140 mm. Hg. When the patient was discharged, he was free from all complaints, but his blood pressure was 160 mm. Hg.

Intermittent claudication

The following case of intermittent claudication showed almost a similar picture:—

Case 9.—Hindu male, aged 50 years, was admitted on 7th October for treatment of hemiplegia of the right side. He was a railway station-master and had sometimes to work on signals with his right hand. Occasionally, he used to experience sudden spasm of the right hand, while working the signals, and was compelled to stop work for a moment. Sometimes at night he used to experience similar spasms and difficulty of stretching his right leg. He had been suffering from these complaints for the last five years. He also gave a history of attacks of malarial fever off and on. A fortnight before his present illness he suffered from dysentery, with 10 or 12 motions a day. On 1st October he was going to his bathroom at 2 p.m., when he suddenly felt that he could not move his right hand and leg, and his speech became blurred. He had to be carried to his bed.

On admission, there was paralysis of the face and right extremities, which were soft and flaccid. The deep and superficial reflexes were present but sluggish. There was flexor response of the plantar reflex. The sensations were intact. His systolic and diastolic blood pressures were 170 and 100 mm. Hg. respectively. Urea-concentration test showed defective elimination of urea, *viz.* 0.8 per cent only in the third sample passed two hours after the load of urea was given. The case was diagnosed as nephro-sclerosis and the paralytic symptoms were assumed to be due to intermittent claudication of a branch of left lenticulostriate artery. Treatment with muscle extract was commenced from 12th October. On 20th October the systolic and diastolic pressures came down to 125 and 75 mm. Hg. respectively. The patient quickly got rid of his paralytic symptoms, the order of disappearance being face, hands and legs.

It will be apparent from a study of cases 5, 7, 8 and 9 that exhibition of muscle extract produced lasting benefit in high blood pressure of nephro-sclerotic patients, but only a temporary beneficial effect in hyperpiesia due to endocrine disorders, and had no effect in reducing blood pressure in advanced arterio-sclerosis. It may possibly be useful in early cases of

arterio-sclerosis, as claimed by Schwartzmann (1831), it probably acting by relieving the spasm of the vasa vasorum and thus ensuring the increased blood supply to the muscular coat of the arteries. The beneficial effect in nephro-sclerosis may reasonably be attributed to the fibrolytic action of the muscle extract.

Mitral stenosis

The fibrolytic action of muscle extract was taken advantage of in the treatment of the following progressive cases of mitral stenosis in which a lasting amelioration of symptoms was achieved. It was given with the idea of stopping the progress of contraction of fibrous scars in the mitral valve:

Case 10.—Hindu female, aged 16 years, was admitted on 4th January, complaining of dyspnoea and palpitations on the slightest exertion, cough, headache, and giddiness. She gave a history of rheumatic fever, while she was a child of 8 years old. Physical examination showed that she was suffering from mitral stenosis. This was confirmed by orthographic mitral configuration, teloradiographic curved impression of the œsophagus caused by hypertrophic left auricle, and electrocardiographic tracings showing broadened and notched 'P' deflections. The patient was put on digitalis and there was some improvement, which however remained stationary. Injections of muscle extract were then given and after receiving two doses, the patient became cheerful and felt better. The complaints quickly disappeared during further injections of muscle extract and administration of digitalis. The patient received ten injections of muscle extract in all, after which she was put to graduated exercise. She left the hospital with vastly improved exercise-tolerance.

Case 11.—Hindu female, aged 22 years, was admitted on 5th January with symptoms of nausea, indigestion, dyspnoea, cyanosis, and expectoration of sanious and frothy sputum. Physical examination revealed signs of aortic incompetence and mitral stenosis. An orthogram showed mitralized aortic configuration and greatly hypertrophied left ventricle. Teloradiographic impression of the œsophagus showed hypertrophy of the left auricle. The Wassermann test was negative. After relief had been obtained from blood-letting and rest, she was given 10 injections of muscle extract. She improved very rapidly. Graduated exercise was then given, and she left the hospital with greatly improved exercise-tolerance on 4th March.

Case 12.—Hindu male, aged 13 years, was admitted on 2nd February with complaints of palpitation of the heart and dyspnoea on slight exertion, for the last three years, after an attack of rheumatic fever. His condition had become gradually worse during the last three months. The case was diagnosed as one of mitral stenosis. Blood pressure was 100/70 mm. Hg. An electrocardiogram showed notched 'P' deflection, low voltage 'R' in all the leads, and less filling of the ventricles. Teloradiographic curvature of the œsophagus was very marked owing to hypertrophy of the left auricle.

Injection of muscle extract was begun on 8th February, and continued in 0.5 c.cm. doses for 10 days. The patient felt more comfortable after each injection. His pulse rate, which was 109 per minute, came down very gradually. However, he developed slight œdema of the legs after the sixth injection, which disappeared after two days. He could not tolerate digitalis at the time of his admission, but when ten injections of muscle extract were finished, he tolerated it very well. After ten days' rest, he was given a second course of muscle extract for ten days. An electrocardiographic tracing showed inverted 'T' wave in the second lead, which ordinarily indicated grave myocardial damage; the

patient however was improving and showed no signs of myocardial weakness or exhaustion. After a few days' rest, a third course of muscle extract was given. An electrocardiographic tracing was again taken and this time the second lead did not show any inverted 'T'

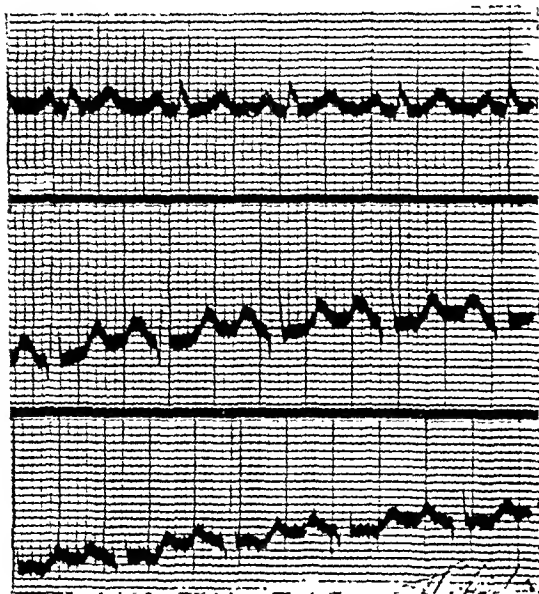


Fig. 1.—(Electrocardiograph taken before exhibition of muscle extract). Rate of heart beat—122 per minute (tachycardia). 'P' notched in all the leads. 'R' low voltage in lead I.

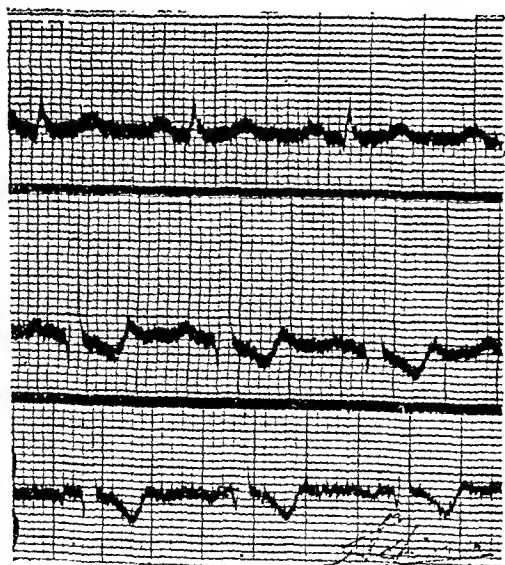


Fig. 2.—(Electrocardiograph taken after two courses of muscle extract). Rate of heart beat—93 per minute. 'P' notched in all the leads. 'R' low voltage in lead I, and inverted in lead III. 'T' inverted in leads II and III.

wave, nor any other abnormality except a notched 'P' deflection due to mitral stenosis. He was discharged on 9th April, with advice to work within the limits of

his exercise-tolerance. I have kept in touch with this patient; he is doing well.

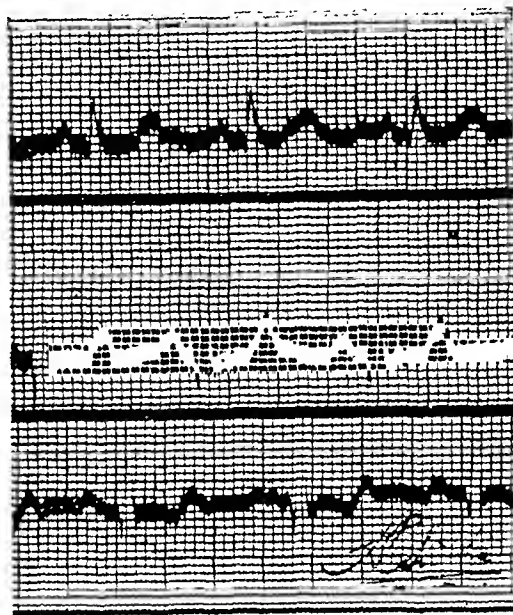


Fig. 3.—(The same case after the third course of muscle extract). Rate of heart beat—88 per minute. 'P' notched and prominent in all the leads. 'R' low voltage but higher than those of figures 1 and 2 in lead I. 'T' positive and prominent in lead II.

Case 13.—Hindu male child, aged 9 years, was admitted on 30th March for treatment of orthopnoea, dry cough, and oedema of the legs and face. He suffered from rheumatic fever two years ago. He had begun to get dyspnoea on exertion since January last; it had gradually become worse. There was a certain amount of bulging of the chest wall over the left precordial region. Teloradiographic impression of the oesophagus showed curvature due to hypertrophy of the left auricle. The case was diagnosed as one of mitral stenosis. An orthogram showed mitral configuration. An electrocardiogram showed tachycardia with broad and notched 'P' wave.

The patient was given Guy's diuretic pill, and magnesium sulphate, and then put on digitalis until the oedema disappeared and dyspnoea was much less. On 10th April injection of muscle extract was commenced and continued for ten days. The patient became cheerful, felt better, and actually wanted to have more injections. On 15th April ova of *Ascaris lumbricoides* were detected in his stool and several worms were passed with the stools after the administration of santonin. On 2nd May the patient took unauthorized walking exercise in the corridor, as a result of which he again became dyspnoeic and suffered from nausea and vomiting. The rate of heart beat went up to 149 per minute. His vomiting was checked by dilute hydrocyanic acid and the rate of heart beat went down after administration of pandigal. A second course of muscle extract was given, and then a third course. He began to make an all-round improvement. He was put to graduated exercises and his exercise-tolerance improved quickly. His weight, which was 44½ lbs. on admission, increased to 64½ lbs. at the time of his discharge on 1st August.

Case 14.—Hindu female child, aged 9 years, was admitted on 9th August for treatment of palpitation, breathlessness on slight exertion, slight swelling of both knee joints and elbows, and pain in the wrists and small joints of the hands. The patient gave a history of rheumatic fever two years ago. Physical signs showed

that she was suffering from mitral stenosis. An orthogram showed typical mitral configuration and radiogram showed curvature of the oesophageal shadow. She was very anæmic, 2,000,000 red blood cells per c.mm. of blood. Her pulse rate was 136 and respiration 34 per minute.

The patient was given two courses of injections with muscle extract. Her complaints disappeared quickly and the pulse rate came down to normal. She was then put on to graduated exercise. Her exercise-tolerance was increased when she was discharged from the hospital on 30th September.

In all these five cases of mitral stenosis, there appeared a lasting amelioration of symptoms of the disease which could reasonably be explained from arrest of contraction and fibrolysis of the scar of the mitral valves. It appears that even physiological scar tissues can be dissolved to a certain extent. This suggestion has been corroborated by observations that in all these five cases of mitral stenosis, there was not only increase of exercise-tolerance but the presystolic thrills became much softer after treatment with muscle extract.

Banti's disease

The muscle extract was tried in the following cases of Bengal splenomegaly (Banti's disease) with the idea of stopping the progress of cirrhosis of the liver which is associated with this disease. The ideal treatment is supposed to be the removal of spleen. De (1932) considers that the cirrhosis of the liver in Bengal splenomegaly is of the multilobular type associated with excessive increase of the connective tissue in the trabeculae, exerting pressure on the radicles of the portal veins and causing ascites. When once this stage has been reached, surgical treatment is of little avail. Again, extensive adhesions of the spleen, a sequel of perisplenitis, makes the removal of the spleen a dangerous operation. Severe anæmia is regarded as a contraindication to operation. It was in these inoperable cases of splenomegaly that muscle extract was tried as an adjunct to deep x-ray therapy of the spleen, with the idea of effecting fibrolysis, allowing the liver cells some time to regenerate and thereby regain some of their lost functions. In one of the following two cases where muscle extract was tried, cirrhosis of the liver with ascites had already supervened, and in the other anæmia was so profound that surgeons would not operate :

Case 15.—Hindu female, aged 20 years, was admitted on 29th February with fever, swelling of the abdomen, anæmia and palpitations. The patient had had two children, the last being born two years ago. She had suffered from hæmorrhage from the uterus for three months. Later, she was attacked with dysentery with 20 to 30 stools a day. She then got swelling of the whole body which gradually subsided, but the ascites persisted. She suffered from frequent attacks of fever and had had no periods since her menorrhagia stopped, that is, for the last year and a half. She was extremely anæmic, erythrocytes being only 910,000 and the leucocytes 4,992 per c.mm. Both spleen and liver were enlarged. The aldehyde and urea-stibamine tests were both negative. Malarial parasites (*Plasmodium falciparum*) were found in the blood. She was treated

with atebirin after which the fever was checked, but there was no improvement in her condition. Her disease was diagnosed as Bengal splenomegaly. As it was an inoperable case, it was proposed to submit the spleen to deep x-ray exposures once a week. Twenty cubic centimetres of whole blood were given intramuscularly twice a week in order to stimulate the hæmopoietic organs depressed by deep x-ray exposures. She was then given 43 injections of muscle extract altogether. She improved slowly, but steadily. At the time of her discharge on 24th June she was completely free from ascites and her red blood cell count was 3,000,000 per c.mm.

Case 16.—Hindu male, aged 20 years, was admitted on 23rd March with a huge spleen, ascites, frequent attacks of fever, and anæmia. The patient was of stunted growth and looked like a boy of thirteen. There was no growth of hair on the face, arm-pits, or pubes. A spleen-puncture smear showed no leishmania. The aldehyde and urea-stibamine tests were negative. No malarial parasites were found on repeated examinations. The case was diagnosed as Bengal splenomegaly with secondary portal cirrhosis and ascites. The number of erythrocytes at the time of admission was 900,000 per c.mm., and the leucocytes were 8,000 per c.mm. The patient got an attack of bronchitis while in the hospital, and on 12th March began to sink into a collapsed condition. Although the patient recovered after getting transfusion of blood, he went down-hill day by day. A course of muscle extract was commenced on 2nd April. The temperature, which was fluctuating all along between 98° to 101°F., gradually touched the normal level and the patient began to improve in weight. The red blood cells increased to 1,900,000 per c.mm.

As this was not a suitable case for splenectomy, deep x-ray therapy of the spleen was started on 14th April with the idea of damaging the mononuclear phagocytes responsible for destroying the red blood cells in the spleen in this disease. The difficulty was that each exposure of x-rays diminished the number of erythrocytes. The red blood cells counted 1,910,000 before the exposure, but went down to 1,700,000 after the exposure. It was therefore decided to give intramuscular injections of 20 c.mm. of whole blood after each exposure. He had 9 exposures of deep x-rays and ten injections of whole blood alternately every week till 28th June. The number of erythrocytes increased to 2,960,000 per c.mm. Ascites disappeared completely. The courses of muscle extract were, however, continued and there was no further manifestation of cirrhosis of the liver in the shape of ascites. The patient gradually gained in weight and was greatly improved in general health. Three further deep x-ray exposures were given alternately with injections of whole blood and, when the patient was discharged on 22nd July, the number of red blood cells was 3,130,000 per c.mm.

Myoclonus

Muscle extract was further given trial to relieve myoclonic twitchings in a case of encephalitis lethargica with progressive bulbar paralysis.

Case 17.—Jew male, aged 53 years, was admitted on 17th September, 1931, to the Ezra hospital with the following complaints:

- (a) aphasia in articulation,
- (b) excessive salivation and difficulty of swallowing food,
- (c) weakness of muscles of the whole body, and
- (d) myoclonic twitchings all over the body.

The patient gave a history of fever a year ago, since when the above complaints gradually commenced and went on increasing. Physical examination showed marked atrophy of the tongue with furrows and fissures, and exaggeration of all deep reflexes. There were progressive paresis of the muscles of the palate and regurgitation of food through the nose. There was increased difficulty of deglutition. The Wassermann

reactions of both blood serum and cerebrospinal fluid were negative.

Treatment with calcium and parathyroid, milk injections, systematic attempts at re-educating his articulation, and iodides failed to improve his condition.

The treatment with injections of muscle extract was begun from 16th January, 1932. It was given intramuscularly in 0.5 c.cm. doses daily except Sundays. Ten injections were given. The myoclonic twitchings diminished remarkably after three or four injections. Salivation was stopped for some time. There was still a good deal of difficulty in deglutition and food still regurgitated through the nose when the patient left the hospital on 5th April.

The quick disappearance of myoclonic twitchings suggests that the action was due to removal of the ischaemic condition of the nerves, probably caused by some spasm of the vasa nervorum.

REFERENCES

- De, M. N. (1932). *Indian Journ. Med. Res.*, Vol. XIX, p. 1029.
 Drury, A. N., and Szent-Györgyi, A. (1929). *Journ. Physiol.*, Vol. LXVIII, p. 213.
 Schwartzmann, M. S. (1931). *Brit. Med. Journ.*, Vol. I, p. 492.

A SEROLOGICAL PROOF OF ETHNOLOGICAL IDENTITY OF THE HINDUS AND THE MOHAMMEDANS OF ASSAM

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[With Comments by H. P. CHAUDHURI, M.B., D.P.H. (Lond.), D.T.M. & H. (Lond.), F.R.S.S. (Lond.), D.O.M.S. (Lond.), Honorary Research Worker, All India Institute of Hygiene and Public Health, Calcutta]

RECENTLY I had an opportunity of testing the blood groups of 2,000 persons. These included men of all castes and creeds, both sick

and healthy; among them were 1,565 Hindus and 355 Mohammedans. The table below shows their distribution according to their blood groups.

It will be seen that there is some difference among the percentages of the various groups, and the question arises whether the difference is of any significance.

Pearson (1911) shows that if we let the population from which the two samples, if undifferentiated, are supposed to be drawn be given by the class frequencies

$$m_1, m_2, m_3, m_4, \dots, m_p, m_q, \dots, m_s.$$

the total population being M , and let the samples be given by the frequencies in the

First sample	f_1	f_2	f_3	\dots	f_p	f_q	\dots	f_s	Total. N
Second sample	f'_1	f'_2	f'_3	\dots	f'_p	f'_q	\dots	f'_s	N'

same classes: where the total N and N' differ widely or little, and then form a quantity

$$\chi^2 = S_1 \left\{ \frac{N N' \left(\frac{f_p}{N} - \frac{f'_p}{N'} \right)^2}{f_p + f'_p} \right\}$$

where S_1 denotes summation of like quantities from 1 to s , that then the required probability that the two samples are undifferentiated, i.e., did come as random samples from the same population, may be found by looking out the value of P corresponding to the ascertained χ^2 and n' (the number of classes) from the tables given on pages 26 to 29 of Pearson's 'Tables for Statisticians and Biometricians'.

	GROUP A		GROUP B		GROUP AB		GROUP O		TOTAL
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	
Hindus ..	390	24.93	498	32.73	145	9.26	532	33.98	1,565
Mohammedans ..	84	23.66	126	35.49	32	9.01	113	31.83	355

TABLE

		Group A	Group B	Group AB	Group O		TOTAL
Hindus ..	(i)	390	498	145	532	f	1,565
Mohammedans ..	(ii)	84	126	32	113	f'	355
(i) + (ii) ..	(iii)	474	624	177	645	$f + f'$	1,920
(i)/1565 ..	(iv)	0.2492	0.3182	0.0926	0.3399	f/N	..
(ii)/355 ..	(v)	0.2366	0.3549	0.0901	0.3183	f'/N'	..
(iv) - (v) ..	(vi)	+0.0126	-0.0367	+0.0025	+0.0216	$f/N - f'/N'$..
Square of (vi) ..	(vii)	0.00015876	0.00134689	0.00000625	0.00046656	$(f/N - f'/N')^2$..
(vii) ÷ (iii) ..	(viii)	0.00000033	0.00000018	0.00000003	0.00000072	$(f/N - f'/N')^2$..
		$= N \times N' \times 0.00000121 = 1,565 \times 355 \times 0.00000126 \approx 0.7060245$					0.00000126
		$= \text{say } 0.7$					

If $\chi^2 \approx 0.7$ and $n' = 4$, then $P \approx 0.801253 = \text{say } 0.8$.

That is to say there are 80 chances to a hundred in favour of the samples being random samples from the same population.

Conclusion.—There are 80 chances to a hundred in favour of the samples being random samples from the same population.

[**Note.**—The writer of this paper appeared to us to have shown originality and ingenuity in his approach of this subject, and, as we did not ourselves feel competent to judge the value of his contribution, either regarding the accuracy of his calculations or the justifiability of his conclusions, we sent his paper for criticism to a senior census officer. He pointed out that there was no reason to suppose that the blood samples from any other group of human beings would not give the same results. He further pointed out the dangers of drawing conclusions from such data, and quoted the example of a scientist who claimed to be able to diagnose pregnancy by some serological test and unfortunately diagnosed it in a sample of blood from a man.

We subsequently referred the paper for further opinion to Dr. H. P. Chaudhuri, Honorary Research Worker, All India Institute of Hygiene, Calcutta, who commented as follows:—

‘Hirschfeld (1919) was the first to suggest that from a study of blood groups it is possible to distinguish the different races of man. He examined the blood of soldiers of different nationalities during the great war; he evolved what is called “the bio-chemical race index” and showed that this was different in different races. Later, Ottenberg (1925) reviewed the work of several authors on this subject and came to the conclusion that with the aid of blood grouping the peoples of the world could be divided into six large groups. More recently, Malone and Lahiri (1929) tried to apply this method to smaller groups in India, such as the Turko-Iranian, Indo-Aryan, Dravidian and others, but found that “the bio-chemical race index” was an inadequate measure as it did not help to bring out clearly the difference or similarity between the different groups of men studied.

Now Dr. Mitra has gone a step further and attempted to establish the identity of Hindus and Mohammedans from a study of their blood groups. He has shown that there is 80 to 90 per cent agreement in the percentage distribution in the different blood groups between Hindus and Mohammedans. The mere fact of this similarity in attributes (that is, blood groups) implies nothing regarding their ethnological identity. In order to establish such an identity it is necessary to obtain information regarding the blood groups of non-Hindus other than Mohammedans, and in the absence of such information it is quite justifiable to contend that 80 to 90 per cent of non-Hindus other than Mohammedans may also show similar blood grouping. Therefore, unless Dr. Mitra produces evidence as to what percentage of non-Hindus, other than Mohammedans, are allied to or different from Moham-

medans, as regards blood groups, his work cannot be considered an important contribution to our knowledge of ethnological relationship of races. Biological tests are indeed of value in the study of racial differentiation, provided we confine ourselves to very broad groups, but, before we can accept results of these tests as evidence in support of racial identity of smaller and more closely-related groups, it is necessary to furnish figures that are above every chance of fallacy. Dr. Mitra has taken great pains in that he has studied over 2,000 bloods, but this does not mean that inadequate evidence and fallacious conclusions are justifiable or admissible.

To support his conclusions Dr. Mitra has sought the aid of a well-known statistical formula called “the chi-square (χ^2) test”. This formula owes its origin to Karl Pearson and is applicable to problems of the kind indicated in the following words by Raymond Pearl (1930): “given two frequency distributions of phenomena, (1) what is the probability on the one hand that the two can be regarded as random samples from the same population whose characteristics are known from the samples only or (2) what is the probability that the one distribution is really different from the other to a greater degree than could reasonably be supposed to have arisen by the operation of chance alone”. Applying this test to Dr. Mitra’s figures one can merely conclude that as regards blood groups Hindus and Mohammedans in Assam are almost identical. It by no means establishes their identity; at most, one may say that it gives an indication that possibly there is some ethnological relationship between the two communities’.—
EDITOR, *Indian Medical Gazette*.]

REFERENCES

- Hirschfeld, L., and Hirschfeld, H. (1919). *Lancet*, Vol. II, p. 675.
Malone, R. H., and Lahiri, M. N. (1929). *Indian Journ. Med. Res.*, Vol. XVI, p. 963.
Ottenberg, R. (1925). *Journ. Amer. Med. Assoc.*, Vol. LXXXIV, p. 1393.
Pearl, R. (1930). *Introduction to Medical Biometry and Statistics*, p. 322. Philadelphia: W. B. Saunders Company.
Pearson, K. (1911). *Biometrika*, Vol. VIII, p. 250.

A Mirror of Hospital Practice

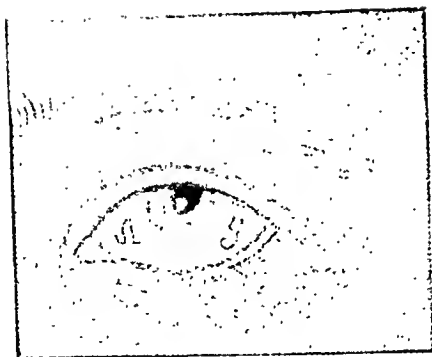
FILARIAL WORMS UNDER THE HUMAN CONJUNCTIVA

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THE first record of a worm in the eye appears to be by Mongin in 1770. *Loa loa* (Guyot, 1778), a human filaria which commonly appears in the eye, is confined chiefly to the west coast of Africa. The adult parasites are smaller than *Wuchereria bancrofti*, have a

PLATE VIII



Showing two worms under the left conjunctiva, one on
either side of the cornea.

truncated cuticle, live in the superficial connective tissue and very frequently appear under the conjunctiva. The embryos, discovered by Manson in 1891, live in the blood stream and exhibit a diurnal periodicity. Manson suggested that a day-biting mangrove fly might be the carrier of this worm and Leiper showed partial development of the embryo in *Chrysops dimidiata* and in *C. silacea*. This was later confirmed by Kleine and by Connal.

The presence of filarial worms in the human eye is a rare occurrence in this country. As far as the author is aware there are only two records of such cases. Charles (1920) reported an adult male, aged 45, resident of Sialkot district, who had a fairly large swelling on the inner and lower side of right eye beneath the ocular conjunctiva. On opening the swelling under local anaesthesia a loop of living worm came out. The whole worm was removed and was later identified by Sewell as probably *Filaria conjunctivae addarioi*, 1885.

The next case was reported by Das Gupta (1921) from Ramporehaut. In a Mohammedan male, aged 25, was found a cystic tumour near the outer canthus. On opening the cyst, 'two fine living worms measuring $1\frac{1}{2}$ inches coiled up together, one slightly larger than the other' were found. They have not been identified.

Recently an interesting case of this type came under my observation. The following are the brief notes on the patient :

Miss M. J., Jewess, aged 16, living in Rawdon Street, Calcutta, since childhood; suffering from elephantiasis of the left leg for the past 4 years. Several members in the family are infected with *Wuchereria bancrofti*. She came to the filariasis clinic on 2nd December, 1932, for treatment of the swelling of the left foot and ankle and she complained of slight dimness of vision in the left eye which had been gradually growing worse for the last seven months on the least eye-strain. On examination, two worms, one on either side of the left cornea, were seen coiled up just under the conjunctiva (see plate VIII). The worms were so prominent that they were visible from a distance. The patient was admitted into the Carmichael Hospital for Tropical Diseases on the same day. One worm was seized with forceps and held during removal of the portion of conjunctiva containing it, by Lieutenant-Colonel Kirwan, I.M.S. As the first worm was being removed, the one lying near the inner canthus disappeared temporarily and reappeared in the original site after 3 days, when it was excised. Neither of the worms could be found although the whole of the portions of conjunctiva removed were sectioned, mounted serially and examined. The patient has been under observation for more than three months since the above operation and the worms have not appeared again in the eye.

Blood examined on several different occasions showed no microfilariae. Total white blood cell count:—8,600 per cubic millimetre. Differential count:—Polymorphs—72 per cent, lymphocytes—17 per cent, mononuclears—5 per cent, and eosinophiles—6 per cent. Stool examination showed scanty *E. histolytica* cysts and *Trichuris* ova.

REFERENCES

- Charles, E. (1920). 'Removal of *Filaria* from under the Conjunctiva' *Indian Med. Gaz.*, Vol. LV, p. 378.
Das Gupta, H. (1921). 'A Case of Filarial Cyst on the Eye'. *Indian Med. Gaz.*, Vol. LVI, p. 338.

A CASE OF TABES DORSALIS IN AN INDIAN

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TABES DORSALIS is sufficiently rare amongst Indians to be worth recording, and the present case presents many typical symptoms.

K. L. A., male, Indian Christian, aged 45, who had never been out of India, was admitted to the ophthalmic ward for drooping of the right upper lid, and was soon transferred to the medical wards.

History.—For two years he had suffered from shooting pains in the lower extremities—described by him as 'electric shocks'—the attacks lasting for fifteen to twenty minutes, and recurring at indefinite intervals of fifteen days to four months, and being experienced mainly in the calves. Coincidentally he had felt a sensation as of a tight rope round his waist at the level of the tenth and eleventh dorsal vertebrae.

For a year and a half he had experienced difficulty in balancing himself, noticed most when washing himself in the morning, for on closing his eyes he would fall forward into the basin.

About six months previously he noticed dimness of vision in the left eye, and at the same time found the right eye deviated inwards and experienced diplopia. He was treated for these troubles in the ophthalmic outpatient department by electric massage and anti-syphilitic measures, though the Wassermann reaction of his blood was negative, both before and after a provocative dose of neosalvarsan. His squint became much better after three months. One and a half months before admission he noticed partial drooping of the right upper lid.

Condition on admission.—A well-built man, who walks with difficulty with a staggering gait, and at once falls on closing his eyes. He complains of frequent pains in his lower limbs, and of the sensation of a continuously present tight band round his waist.

Cranial nerves.—The right eye is slightly deviated outwards and the right upper lid droops slightly; the internal movement of the right eye and external movement of the left eye are defective; the pupils are unequal, the right being the larger; the right pupil does not react to light but reacts sluggishly to accommodation; the cilio-spinal pupil reflex, while present in both, is very sluggish in the right eye; the consensual light reflex is present in the left eye only; Wernick's hemianopic pupil reflex is not present; vision is 6/6 in both eyes; fundus examination shows no abnormality.

Outside the eyes the only cranial nerve abnormality is a weakness of the right facial muscles.

Upper extremities show no change, motor or sensory.

Lower extremities show defective co-ordination, but normal motor power. Sensations of heat, cold, touch, and pinprick are normal, but muscle sense and vibration sense are absent in legs and feet. The deep reflexes are completely absent, and the plantar reflex gives no response.

Trunk.—No area of anaesthesia could be found, band or other.

Blood.—Wassermann negative.

Cerebro-spinal fluid.—Wassermann strongly positive. Cell count 25 per cm.

The diagnosis cannot be doubted. Treatment by intra-thecal injections of salvarsanized serum by Swift Ellis' technique were commenced. The patient was given an injection of 0.6 gramme neosalvarsan. Twenty minutes after this about 30 cubic centimetres of blood was withdrawn, to yield some 15 cubic centimetres of

serum. The blood was kept overnight in an ice chest, and next day was centrifugalized and the clear serum pipetted off and made up to 30 cubic centimetres by the addition of normal saline. The salt-serum mixture was kept for half an hour in a thermostat.

Lumbar puncture was performed in the lateral position, and 25 cubic centimetres of cerebro-spinal fluid withdrawn; 30 cubic centimetres of the salt-serum mixture was then introduced through the needle, so as to diffuse under pressure. Two such injections were given, with about two weeks interval; after each one, at about four hours interval, the patient experienced lightning pains of the severest type, with increase of the girdle sensation, so severe as to demand morphia in full doses. The pains lasted about six days. The patient removed himself from hospital without more treatment.

A CASE OF FIBRO-LIPOMATOSIS ASSOCIATED WITH FEVER

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R. D. P., male, aged 24 years, was transferred to this hospital at the end of November 1932, being under artificial pneumothorax treatment for pulmonary tuberculosis, with the history of recurring attacks of high fever not apparently attributable to the tuberculous infection.

He was a lad in fairly good general condition, with one lung collapsed and the other clinically and radiologically healthy, and no signs of disease elsewhere. He ran an intermittent temperature from 30th November to 12th December of 101°F. to 104°F. each evening, the morning record being normal. The fever was neither preceded by rigor nor followed by sweating. From the beginning the patient insisted that the fever was connected with the appearance of small nodular swellings under the skin, and pointed out a number of what appeared to be fibro-lipomata, but at first not much importance was attached to his statement.

On the 8th January the temperature again rose to 101°F., and the patient called attention to a small nodular swelling on the left forearm which, he said, had just appeared, and this swelling was carefully watched. It started as a painful red indurated area with pain on moving the limb; in a few days in this area a firm painless nodular mass was felt, about the size of a small pea; this slowly increased in size for three or four days and then remained stationary. Meanwhile similar nodules had appeared elsewhere. The swellings ceased to appear in about a week and the temperature settled down on the 16th, having ranged daily from 101°F. to 104°F.

On the 30th January the patient again had a short attack of fever of milder intensity, accompanied by the appearance of more swellings, the first being on the posterior aspect of the left leg.

Altogether, during approximately two years, about eighty swellings had appeared in different parts of the body, and could be felt as small firm subcutaneous masses, movable and painless, and resembling those seen in von Recklinghausen's disease. The patient said he could foretell each attack of fever by the appearance of these swellings.

During this period the treatment by artificial pneumothorax was maintained with clinical success.

The following pathological findings were made:—

The blood, urine and feces were normal, and no parasites were found. Histological examination of one

of the swellings showed the structure to be a fibro-lipoma.

Though different forms of fibro-lipomatosis have been described including that of von Recklinghausen, and some are painful, we cannot find any record of the appearance of such growths accompanied by attacks of fever. Clinically they resembled molluscum fibrosum, though none of them were larger than an almond. The nodules in *tuberculosis dolorosa* are painful, but are usually neuro-fibromata: these nodules were not painful after they had ceased growing, and the histological examination revealed no nervous tissue.

The patient left hospital in mid-February for a sanatorium.

A CASE OF CUTANEOUS PLAGUE

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A HINDU, aged 22 years, a student, was admitted to hospital with a history of high fever for the past four days and an acute spreading ulcer on the left side of chest wall which started as a pustule two days after the commencement of the fever. There was no history of proximity to plague infection.

A hard mass about the size of an almond was situated about 4 inches above the ulcer. In spite of energetic local and general treatment his condition became worse and three days after admission two more ulcers appeared near the first one.

The margins of the ulcers progressively extended giving the appearance of large areas of gangrenous integument with a tendency to surrounding bleb formation suggestive of the toxins of *Bacillus oedematis*. So anti-gas gangrene serum 4,000 units was injected. By this time the patient was very seriously ill.

Smears taken on the fifth day were reported by the pathological department to contain *B. pestis* and this was subsequently confirmed by animal experiments.

A week after admission the patient was delirious with subsultus tendinum—condition very low—ulceration greatly extended—covering an area of about one square foot—exuding foetid discharge, enlargement and tender masses of glands in the cervical, femoral and epitrochlear regions on both sides.

On the following day the left eye became acutely inflamed; this ended in complete destruction of the cornea from ulceration causing total loss of vision.

After a protracted convalescence in which the femoral gland buboes had to be opened and drained the patient was finally discharged from hospital cured, two months after admission.

A few points of interest about this case are:—

(1) An exact description of the ulcers appears in *Manson's Tropical Diseases*, ninth edition.

(2) On admission, although the patient gave a history of four days' illness, he did not look at all ill.

(3) Despite the presence of the ulcers on the chest wall there were no buboes or enlarged glands present on any part of the body until the twelfth day of disease.

(4) Keratitis which resulted in total loss of vision in the left eye is a rare complication.

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Indian Medical Gazette

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TRAINING FOR MATERNITY AND INFANT WELFARE WORK

ONE of the most hopeful omens for India's future is the increasing interest that her sons and daughters are displaying in maternity and infant welfare work. Though pioneer workers organized centres in a few of the larger towns and in certain model village settlements some years ago, it is only during the last five years or so that the interest in this form of social service has become widespread and reached the rural areas. It is unfortunate that this sign of the quickening of the social conscience in India should have been so timed that its infancy will have to be passed in a period of great financial depression. The survival of this movement will depend on the determination of its supporters and the next few years will show whether it was a passing phase of nationalistic enthusiasm or a genuine appreciation by the educated classes of their duty to the masses.

Hitherto the organization of this work has been a matter of personal local effort and, though in certain cases governments and municipalities have given grants in aid, most of the money expended has had to come from the pockets of the active supporters of the movement or from those of their friends. This is the history of welfare movements in other countries and, although when the value of the movement has been established and when money is less scarce the whole organization may be financed from public funds, it is a state of affairs in which, in the present circumstances, there is nothing intrinsically wrong; a social conscience which urges a man to sit down and write to the papers demanding that the government shall do something about it, but does not stimulate him to make some personal effort is barely worthy of the name. In India the government spends a greater proportion of its total revenues on medical relief, by the provision of free hospital and dispensary treatment, and on public health measures, than is the case in many other countries. The contention of the sanitarian is that by public health measures rather than by the temporary amelioration of the symptoms of the individual—which is often all that hospital and dispensary treatment can hope to achieve—the most lasting benefit to the community is likely to be effected, and that therefore this should be the first consideration of the government. At the present time this is not the case; a much greater sum is expended on

the provision of hospitals and dispensaries than on preventive measures. This is a point of view with which we are in entire agreement, but it is not the popular one; the demand is for more and more hospitals and dispensaries. In these circumstances a wholesale deflexion of public funds from the medical relief budgets to the public health (or prevention) budgets would be very unpopular, and is therefore out of the question, *until the people have been taught by demonstration to appreciate the value of preventive measures.* We will return to this point later; meanwhile we will refer to some of the requirements, and some of the shortcomings, of the present-day welfare organizations in this country.

Voluntary workers have little sympathy with the collection of statistics; they consider them as a form of official red tape which they in their 'voluntary' capacity are lucky to be able to avoid. On the other hand the trained public health worker knows that schemes of work follow, not precede, the proof of the necessity for them, and that in the absence of reliable statistics it is impossible to determine what is the most urgent need and what form of public health measure will bring the greatest advantage to the largest number of people.

Statistics for the incidence in and death rate from certain epidemic diseases throughout India are available and, although it is fully realized that these are not correct in detail, it is generally accepted—and we think quite rightly—that they give a very fair indication of the relative incidence of these diseases year by year and district by district. However, maternal mortality statistics are notoriously incorrect everywhere. Bombay, which has a special municipal order relating to maternal deaths and is therefore probably above the average as regards accuracy in this respect, will serve as an example.

The following figures are taken from the 1931 report of the Medical Officer of Health for Bombay:—

Number of births	Number of maternal deaths	Maternal mortality
27,204	198	7.2

The two largest maternity hospitals in Bombay together report 171 maternal deaths *plus* 9 deaths due to general diseases associated with pregnancy in a total of 6,767 births, a maternal mortality rate of 25 per mille. This leaves a balance of 27 deaths amongst 20,427 births in other hospitals and in the general population; this is of course ridiculous. Further discrepancies will be found if we look into the causes of death. These are given below in tabular form. The percentages have been calculated and the corresponding figures for England and Wales given for comparison.

Cause of death	BOMBAY				ENGLAND AND WALES
	M. O. H's. REPORT		HOSPITALS		
	Number	Percentage	Number	Percentage	Percentages
Anæmia of pregnancy	17	8.6	43	23.9	..
Sepsis	93	47.0	36	20.0	37.1
Eclampsia and other toxæmias	39	19.7	14	7.8	17.6
Operative shock	11	5.6	8	4.4	9.9
Hæmorrhage	21	10.6	16	8.9	14.3
Other diseases	17	8.6	63	35.0	20.8
Other accidents of pregnancy					
TOTALS ..	198	..	180

That is to say 17 persons are reported as having died of anæmia of pregnancy in the whole of Bombay and yet 43 died of this condition in two of the hospitals in the city; further comment is unnecessary. Incidentally this table emphasizes the importance of anæmia as a cause of death in the Bombay hospitals, as compared with sepsis and would appear to indicate the importance of antenatal care rather than improvement in midwifery practice as a means of reducing the death rate, but it is obvious that when registration and returns are so palpably inaccurate they cannot be used as a guide to action.

Bombay has been taken as an example because it has special arrangements regarding maternal death registration and yet the figures are demonstrably incorrect; the same unreliable information (or no information whatsoever) is all that is available in any part of India on a subject of such vital importance to the nation as the health of the mother and her baby. Information on the subject of infantile mortality is equally defective and misleading. The figures available give the infantile mortality in various places in India as varying between 137.8 (Bihar and Orissa) and 329 (Lucknow); the rate in Calcutta, for example, is 278. A health visitor kept a record of all the births and deaths occurring in the lines of a jute mill for a period of five months; during this period there were 63 births and 19 of the infants died, of which 16 died in the first month; making allowances for the fact that only half the deaths in the last month would be recorded, these figures indicate a mortality rate of 282 per thousand births, in the first month of life. The causes of death included tetanus neonatorum in five instances, heat stroke in three, and other equally avoidable conditions. The cause of this appalling mortality is not only the lack of suitable medical and nursing provision, but is also the result of social custom and prejudice, and demonstrates the necessity of carrying the teaching of the fundamental principles of

cleanliness and fresh air into the homes of the people, who are too fatalistic, too careless of human life and too indifferent to suffering to seek enlightenment for themselves.

Epidemic diseases, on account of the dramatic severity of their onset and the number of deaths they cause in a short time, arouse public attention and lead to a demand for relief and even preventive measures; but epidemic diseases come and go; pregnancy and labour we have with us always. There are in India over eight and a half million childbirths yearly, but the incident is so familiar in our daily lives that we give little thought to its consequences, yet the sum total of unnecessary deaths and disablements that result over a period of ten years must rival the ravages of any single disease, with the possible exception of malaria, over the same period. Public health authorities are but servants of the public and, though they play a very important part in educating the public, meanwhile they are to a certain extent compelled to direct their activities where public opinion demands them. If the number of maternal and infantile deaths in which an avoidable factor plays the major part could be estimated, the public conscience would be stirred. Hitherto the organizers of the welfare movement have not made the most use of their opportunities to obtain accurate figures on these subjects; the reason for this is that they are in most cases untrained and have not the knowledge or the appreciation of the value of vital statistics so essential for all welfare workers.

Many welfare schemes fail to make the most of their opportunities by attempting too much. The cause of this defect lies in the preponderating humanitarian outlook of the voluntary worker who wants to bring relief—and immediate relief—to the largest number of persons possible. We can sympathize with this point of view although it usually leads to the misdirection of effort and little permanent benefit. Welfare schemes should have as their objective the raising of the standard of physical and

mental health of the community; to confine their activities to restoring and maintaining the health of a few scattered individuals by the giving of medicine, milk and baths is to fail to keep this objective in view. The weaning of the people from their old-established and insanitary customs and practices alone will raise the standard of public health, and an intensive educational campaign, through the maternity and child-welfare organizations and health education in schools, with this end in view is the duty of the health department of every province. Mere reiteration of health precepts will, however, be insufficient to convince the people and practical demonstrations will form an essential part of such a scheme. The present lack of trained personnel, not to mention financial considerations, make comprehensive schemes out of the question, and the choice lies between indifferent work over a wide area and intensive work in a limited one; the latter is obviously preferable from all points of view because it provides more striking results for the education of the people, as well as a better opportunity for obtaining a proper estimation of the value received for the money expended.

The provision of trained personnel for directing welfare schemes is beyond the powers of the voluntary organizations who quite rightly look to governments and local authorities for help in this direction. Certain progressive municipalities are initiating schemes and with the return of prosperity others are bound to follow suit. Then, the real tragedy of the present position in India, the lack of properly trained medical personnel will become more and more apparent. Many schemes, excellent in conception, fail in execution because the staffs appointed to administer and carry out the work lack the preventive outlook. Prevention is invading the medical curriculum, so long the stronghold of curative medicine, but the whole bias in practical training is still towards the recognition, the study and the cure of established disease, and it is futile to expect the doctor, taught on these lines, to give up immediately the only methods he (or she) knows, in favour of the study of health, and of its promotion by education and advice in environmental and personal hygiene. The medical officer of health is not called upon to organize the health services of a province or city without being specially trained for the work, and it is absurd to expect a doctor who has no idea how to survey an area with regard to its public health needs, who knows nothing of the cost of, or how to train, the necessary staff, and who knows nothing of vital statistics, of epidemiology, or of public health law, to organize and administer a maternity and child-welfare scheme, when perhaps his only idea of welfare work is vaguely that its object is to reduce the infantile and maternal death rates, and when he is incapable of visualizing the distant goal of racial betterment through the teaching of

hygiene, eugenics and population control. It is futile to expect that he, or she, will even make a good executive officer, supervise the work of the health visitor and midwife, train the dai, or advise with authority on breast and artificial feeding and on the upbringing of difficult children, when the opportunity for the study of child physiology, children's diseases and child psychology are as limited as they are to-day in most Indian universities.

To meet the needs of the provinces and larger towns for administrative and executive officers for maternity and infant welfare, a diploma course in the subject is, we understand, being arranged at the All-India Institute of Hygiene and Public Health in Calcutta. The syllabus will probably be similar to that for the diploma of public health, the chief difference being the omission of subjects, such as sanitary engineering and public health physics, and the provision of more opportunity for lectures and practical work in advanced midwifery, infant care and management, child psychology, school hygiene, the organization of child-welfare schemes, and similar subjects.

A section for maternity and child-welfare and school hygiene was one of the six sections included in the original scheme for the All-India Institute of Hygiene and Public Health, but unfortunately it is not one of the four sections that the Government of India has decided that in the present circumstances they can afford to finance. However, so important do the managing body of the Women's Medical Service consider the provision of skilled services for the protection of child life and health amongst the various plans for national advancement, that they have deputed a member of the service to organize the department and to inaugurate a model welfare scheme where the practical training in connection with the diploma may be carried out. It is hoped that government sanction will be obtained for the opening of the course in October under her direction.

The outstanding need for the welfare of the mother and child in India to-day is a body of trained medical men and women to reorganize existing welfare schemes and to institute a programme of steady extension of this work throughout the whole country. The commencing of this course at the All-India Institute in Calcutta will provide the opportunity for meeting this need. We have little doubt that there will be a sufficient number of candidates for this course, and the responsibility for the full attainment of the object of its institution will now fall on the various provincial governments, municipalities and other public bodies to provide training scholarships and thereafter suitable posts and opportunities for the successful candidates to put their knowledge into practice; if they do so, the maternity and infant welfare movement in India will have been placed on a sound foundation.

Medical News

FORLANINI

At the two conferences of the International Union against Tuberculosis held in Rome in 1928 and in Oslo in 1930, it was decided to open in all countries a subscription on behalf of a monument to the memory of Forlanini.

The inventor of the artificial pneumothorax not only endowed medicine with the first really active and efficient method for the cure of tuberculosis, but his discovery paved the way to all the collapse-therapy methods with which medicine is to-day fully armed to overcome this disease.

All patients and physicians in India will, we feel sure, be pleased to have this opportunity of showing their gratitude to this illustrious son of Italy. Even the most modest donation, as well as a larger contribution, will be welcome. This appeal has reached us through the Comité National de Défense contre la Tuberculose, which has undertaken to collect the French donations, and the Indian Red Cross Society which has undertaken to collect those from India and to forward them to the right quarter. In these times one cannot expect large donations, but the object is to make the memorial an international one and it would be a pity if India did not contribute her share. We therefore appeal to all physicians, and through them to their patients, particularly those who have received benefit from this form of treatment, to answer this urgent appeal for subscriptions to Forlanini's memorial.

UNITED PROVINCES MEDICAL COUNCIL

THE Registrar of the United Provinces Medical Council has forwarded to us the following extract from the minutes of the meeting of the United Provinces Medical Council held on 1st May, 1933:

The letter of Dr. T. N. Varma, regarding medical officers in Government service writing prescriptions on printed forms supplied by certain chemists and druggists, was read.

Resolved that this Council looks with strong disfavour on the practice of medical practitioners writing their prescriptions on forms supplied by chemists and druggists bearing their name and address, and advertisement.

Further resolved that this decision of the Medical Council should be sent for publication to daily papers, the vernacular papers and the medical journals.

INDIAN MEDICAL BIRTHDAY HONOURS, 1933

THE following are the names of medical men and others associated with medical institutions in the Indian Honours List of date 3rd June, 1933. We would offer them our congratulations:

Knighthood

Colonel R. McCarrison, Indian Medical Service, an officer of the Indian Research Fund Association.

Dr. Kedar Nath Das, Principal, Carmichael Medical College, Calcutta.

C.I.E.

Brevet-Colonel James Macpherson, Residency Surgeon, Bangalore.

Lieutenant-Colonel W. L. Harnett, Professor of Surgery, Medical College, Calcutta.

Dr. J. N. Duggan, Professor, Grant Medical College, Bombay.

O.B.E.

Dr. E. D. Shroff, Health Officer, Karachi Municipality.
Captain M. R. Sinclair, on special duty with the Political Officer, Sikkim.

Kaiser-i-Hind (Gold Medal)

Mrs. L. M. Hope, Medical Practitioner, Bengal.
Lieutenant-Colonel S. G. S. Haughton, Indian Military Hospital, Quetta.

Kaiser-i-Hind (Silver Medal)

Miss Mary Clare Albuquerque, Medical Officer, Maternity Hospital, Bangalore.

Miss Janet Alexander, Lady Doctor, Mission Hospital, Montgomery, Punjab.

Miss Sarah Love McRobbi, Superintendent, Memorial Hospital, Fatehgarh, U. P.

Miss S. J. Rankine, Assistant Medical Officer, St. Margaret's Hospital, Poona.

Khan Bahadur

Dr. Abdul Qaiyum, Provincial Medical Service, Officiating Civil Surgeon, Manbhum, Purulia, Bihar and Orissa.

Rao Bahadur

Dr. Rajangam Siva Subramania Aiyar, Civil Surgeon, Insein and Hanthawaddy Districts, Burma.

Dr. K. R. Thampi, Inspecting Medical Officer (Retd.), Travancore.

Khan Sahib

Dr. Kahir Hossain, Bengal Medical Service, Senior Teacher, Medical School, Jalpaiguri, Bengal.

Dr. Haji Bashiruddin Ahmed, Sub-Assistant Surgeon, at present posted as Medical Officer in charge of Bongaon Sub-division and Dispensary, Jessore, Bengal.

Dr. Abdul Majid Khan, Provincial Subordinate Medical Service, Medical Officer in charge, Baghpatt Dispensary, Meerut District, U. P.

Rai Sahib

Dr. Adhar Nath Sanyal, Medical Officer of Health, Farrukhabad, U. P.

Dr. Suraj Mal Sarien, Chief Medical Officer, Dholpur State, Rajputana.

Rao Sahib

Dr. Y. G. Vasudeva Ayyar Avargal, District Health Officer, Salem, Madras Presidency.

Dr. S. Kumaraswami Pillai, Avargal, Civil Surgeon, Madras Presidency.

Dr. Rajaram Dattopant Parulkar, Medical Officer of Health, Bijapur Municipality, Bijapur.

Dr. Jhalashankar Samapdas Shad, Chief Medical Officer, Wankanner State.

FIFTY YEARS AGO

(From the *Indian Medical Gazette*, July 1883)
Précis of Operations performed in the Wards of the first Surgeon, Medical College Hospital, Calcutta, during the year 1882.

Lithotomy.—Mahomedan male, æt. 60; symptoms of 3 years' duration, urine alkaline, traces of albumen. Left lateral lithotomy performed; bilateral section of prostate made, stone weighed 1 oz. 6½ drs.; made a good recovery in 37 days.

* * * * *

Lithotrity.—Mahomedan male, æt. 36; symptoms of 2 or 3 years' duration. Stone crushed on three occasions, on 3rd, 10th, and 14th of March; suffered from a smart attack of fever after the first operation; very little vesical irritation. Remained 44 days in hospital.

* * * * *

Plastic operation for restoration of lip.—Hindu male, æt. 30. Had suffered from a carbuncular boil of lower lip 4 years ago, 6 teeth and a corresponding length of gum exposed. A flap was taken from the chin and transplanted upwards. This served to supply the deficiency and conceal the teeth and gums. Remained 22 days in hospital.

Change in the size of the red corpuscles.—Mensuration of the corpuscles was effected by drawing with the

aid of a camera lucida ten corpuscles, and then calculating their mean diameter.

The size of the red corpuscles in health is a tolerably constant quantity—the diameter usually given in the textbooks ranging from $1/3,500$ th to $1/3,200$ th of an inch, that is from 7.3μ to 7.9μ . Cornil and Ranvier give the mean diameter as 7μ

* * * * *

That the red corpuscles do not always contain a constant quantity of hæmoglobin was conclusively demonstrated by Johann Duncan in 1867; and has since been amply confirmed by Malassez, Hayem and many others.

The several clinical methods devised for determining as accurately as possible the relative quantity of

hæmoglobin in the blood all agree in the principle of contrasting a solution of blood of known strength with certain standard colours or coloured substances corresponding to the tint of a solution of normal blood. Of the different instruments the simplest and readiest of application is Gowers's* modification of Malassez's original apparatus, where the standard of comparison is tinted glycerine-jelly made to represent the colour of 20 cubic millimetres of normal blood diluted 100 times—thus allowing of the amount of hæmoglobin, in the blood which is examined, being stated in terms of a percentage with reference to normal blood. Gowers's hæmoglobinometer was used for the present series of observations.

* Vide *Lancet*, p. 822, Vol. II, 1878.

Current Topics

The Modern Conception of Nephritis

By T. IZOD BENNETT, M.D.

(Abstracted from the *Lancet*, 7th January, 1933, p. 8)

ALL those who have been engaged in the active practice of medicine during the last 20 or 30 years must agree that there has been an astonishing change in the precision with which a diagnosis can usually be established. However much one may reverence the experience and clinical instinct of the great physicians of the last century and the epoch immediately preceding the war, it would be foolish to pretend that they were capable of identifying and classifying disease in a manner in any way approaching what is possible to-day. If we reflect on what would happen during a teaching round in a medical ward before the war, we remember most brilliant teachers arriving at conclusions which were often accurate as regards the broad nature of the disease, and not infrequently genuinely precise when the post-mortem room revealed the ultimate details, but the contrast between this and a visit to the wards of a modern hospital is really very great. To-day you will go to such a ward and see, for example, a series of cases of this description—an ulcer on the lesser curvature of the duodenal cap, a case of pernicious anæmia, with the blood nearly restored to normal but with subacute combined degeneration of the cord, a case of pulmonary tuberculosis with the disease confined to the right apex, a case of sacro-iliac strain, a case of carcinoma of the fundus of the stomach, a case of tetany due to chronic steatorrhœa, a case of hypertensive cardiac failure with auricular fibrillation, a case of dysphagia due to achalasia of the cardia, a case of diverticulitis with recurrent pain and pyrexia. These are everyday cases, and the point which I wish to emphasize is that you will find precise diagnosis established in every one of them to-day, whereas 15 years ago this was not possible, at any rate as a rule.

I do not wish to imply that this is entirely due to laboratory methods and the help of x-ray examination; it is very largely due to these things, but actually precision is often reached to-day through the more exact knowledge which experience, gained by the help of these ancillary services, has given us.

KNOWLEDGE OF NEPHRITIS

When we come to nephritis it must at once be admitted that there are, in spite of the brilliant work of a host of investigators, enormous gaps in our knowledge which prevent us from achieving that precision which exists with regard to many other common diseases. Anyone accustomed to survey the world's literature dealing with nephritis is aware of considerable divergence of opinion, sometimes between country and country, and even more often between different authorities in the same country. At the same time, I would suggest to you that the last five years have

seen the emergence, in many different countries, of an important agreement concerning the major aspects of nephritis amongst a body of workers who have studied the subject deeply, sometimes in collaboration, sometimes independently. These workers, amongst whom I would include Fishberg, van Slyke, Epstein, and Addis in the United States, Achard in France, Volhard and Fahr in Germany, Snapper in Holland, and Gainsborough and others in this country, are steadily reaching close agreement as to the classification of nephritis, both as regards its clinical course, its ætiology, its morbid anatomy, and its biochemical manifestations, and although I think not one of them would suggest that anything approaching finality has been reached, they nevertheless represent an agreed conception concerning the general features of nephritis which is something quite new in the long history of medical inquiry into this subject.

I cannot put before you more than a somewhat fragmentary outline of the major points in this conception, but some of these will, I think, be of value in deciding when, and in what manner, a person with a history of nephritis, or with evidences pointing to nephritis, can be accepted by the examiner for life insurance.

RENAL FAILURE

The first conception to which I would draw attention is that of 'renal failure'. By this we mean a condition in which so great a proportion of the total kidney substance is temporarily or permanently out of action that the physiology of the body is deranged.

The normal kidney is made up of a vast number of individual units, each of which begins in a glomerulus; nature has provided far more of these units than are essential for life; it is a common observation that half the total kidney substance—i.e., one of the two kidneys—may be lost without permanent impairment to health, and we know that actually between two-thirds or three-fifths of the total kidney substance must be out of action before renal failure is established. A useful analogy may be drawn between renal failure and cardiac failure; each of these conditions may be temporary or permanent, and each of them may be compensated or decompensated. Just as toxæmia may produce acute cardiac failure from which the patient ultimately recovers, so an acute nephritis may produce a condition of renal failure which is not by any means necessarily permanent or fatal. As regards compensation, the analogy is less exact because long-standing compensated renal failure is a much rarer phenomenon than compensated cardiac failure, and is seldom compatible with prolonged good health.

The conception of compensation and decompensation in renal failure depends on recognizing that the main function of the kidney is the elimination of those superfluous chemical products which are found in the urine.

nitrogenous matter, particularly urea, being the most important. In order that the elimination of these bodies may be accomplished with a minimal loss of water the kidney has the power of concentrating many of them in such a way that normal urine exhibits an enormously greater concentration of urea than does the blood. The damaged kidney shows its failure first of all by a loss of this concentrating power; it still succeeds in eliminating the daily quota of urea and other substances, but can only do this by pouring them out together with considerable amounts of water. In consequence of this we have polyuria as the first sign of renal failure, and this polyuria is a compensatory process because the kidney is still fulfilling its major function of maintaining the blood chemistry practically constant. If renal failure persists the kidney becomes unable, even with the aid of increased water excretion, to rid the blood entirely of excess of urea. Uncompensated renal failure is then present and change in the blood chemistry can be demonstrated, this change being most often in the form of an increase in the urea and non-protein nitrogen. The following table represents the main findings in compensated and uncompensated renal failure:—

		RENAL FAILURE	
		Compensated	Uncompensated
Urine {	S. G. ..	Never above 1020	Seldom above 1015
	Urea ..	Below 2 per cent	Below 1.7 per cent.
Blood	Urea below 40 mg.	Urea 40-300 mg. N.P.N. 40-300 mg.
Symptoms	Polyuria	Polyuria. Gastro-intestinal symptoms.

It must next be emphasized that renal failure is a disturbance of function which may occur in any form of renal disease. It may occur during an acute nephritis or as the termination of a chronic nephritis, or it may occur in such conditions as damage to the kidneys from prostatic obstruction, polycystic disease, or tuberculosis of the whole urinary tract. It is a clinical state and not a disease in itself, and the prognosis, when it is present, depends on the disease causing it and the therapeutic possibilities which such disease may exhibit.

URÆMIA AND PSEUDO-URÆMIA

The understanding of the conception of renal failure is important because it is now considered that uræmia is explicable by the ancient conception of Bright—namely, that it is a chemical intoxication largely due to the accumulation of urea in the blood. For several generations this conception has been rejected because of the frequency of persons dying with obviously diseased kidneys but without any notable increase in the concentration of urea and non-protein nitrogen in the blood. Observers therefore sought for some toxic substance other than urea which might be the principal agent producing uræmia, and it was commonly believed that nitrogen retention, when present, was merely an index of disordered blood chemistry, and that the unknown toxin responsible for uræmia might be present in the absence of these other signs. To-day it is believed by the group of workers to whom I have referred that the term uræmia should be reserved solely for those cases in whom there is gross nitrogen retention. We recognize a condition of compensated renal failure in which there is a normal blood chemistry maintained by the mechanism of polyuria; we next recognize a condition of uncompensated renal failure with polyuria but with an increasing concentration of urea and other chemical substances in the blood; and, finally, we recognize a condition of true uræmia in which the blood-urea has become enormously elevated, giving figures

always above 150 mg. per 100 c.cm. and usually in excess of 200.

This condition of true uræmia is characterized by gastro-intestinal disturbance and deepening coma. Other manifestations, air-hunger, twitching, and so forth, often accompany it, but these are not essential; they are the results of varying secondary changes in the blood chemistry, such as lowering of the alkali reserve and hypocalcæmia. If I were asked for the most characteristic clinical sign of true uræmia I would say that it is the occurrence of a metallic or ammoniacal taste in the mouth due to the presence of large quantities of urea in the saliva, and not infrequently recognized as such by the patient.

If this is true uræmia, what is the explanation of the many fatal cases of coma without changes in the blood, but with obvious renal disease at autopsy? The answer is that these latter are examples of pseudo-uræmia in whom renal disease is accompanied by changes in the cardiovascular system, and that it is this cardiovascular change which produces cerebral effects leading to coma and death. It is often a matter of considerable difficulty to distinguish between the two groups on clinical examination alone. The pseudo-uræmic group is always characterized by elevation of the blood pressure, whilst the evidences of chemical derangement are slight or absent. The fact that these cases are dependent on changes in the lesser arteries and on diminution of the blood-supply of the brain leads to the fact that changes in the retina are present in most of them, chemical changes in the blood and urine are not conspicuous and may actually be absent. In true uræmia, on the other hand, there may be no elevation of the blood pressure at all, eye changes are often absent, but examination of the blood invariably discloses the true diagnosis.

From the therapeutic standpoint the distinction between these two conditions is of the utmost importance, because in true uræmia the indication is to adopt measures such as protein starvation which may alleviate the chemical condition of the blood, whereas in pseudo-uræmia it is of cardinal importance to bring about a change in the cerebral circulation as rapidly as possible, and venesection, lumbar puncture, and the intravenous administration of hypertonic solutions often become of critical importance. A. M. Fishberg, of New York, who has done so much invaluable work on these questions, has also been responsible for the introduction of many felicitous terms which enable us to understand the modern view. He refers to the cerebral manifestations of high blood pressure as 'hypertensive encephalopathy' and he would have us speak of 'hypertensive retinopathies' in all those conditions where changes of the retina occur in the course of disease or the cardiovascular system include those examples where the kidney is also involved. Surely this is a change well worthy of general adoption. At a time when we know full well that the group of cases in which albuminuria is most conspicuous, that is to say in the nephroses, retinal changes are never observed, it is ridiculous to retain the term 'albuminuric retinitis' for a condition which clearly has no necessary connection with the presence of albumin in the urine.

THE CLASSIFICATION OF NEPHRITIS

I have felt it necessary to bring before you the above considerations because of the confusion between renal failure and true and false uræmia. The classification of nephritis, because I feel that a clear conception of these states is essential for an appreciation of the classification of nephritis which is becoming evolved largely as a consequence of such doctrine.

I hope that I may be forgiven if at this point I interpolate a brief account of classifications of nephritis which have found many adherents in the past, some of which are current at the present date.

It is impossible to approach the subject of classification without reference to the past, and I must remind

you that Bright was exceedingly cautious in avoiding any hard-and-fast differentiation into groups. Study of the medical history of the last century indeed emphasizes the lack of uniformity in teaching, although it was perhaps unfortunate that in the absence of unity of conception individual writers tended to be dogmatic in dividing renal disease into various groups. It was largely as the result of the work of Wilkes and of Bartels that it became customary to distinguish two main varieties of chronic nephritis to which were attached the terms 'chronic parenchymatous nephritis' and 'chronic interstitial nephritis', the former being essentially a condition characterized clinically by dropsy and albuminuria, and the latter one in which there was a small contracted kidney in a patient dying of uræmia or cerebral hæmorrhage without œdema. The supposed occasional transformation of a case belonging to one group into a condition which flung him into the other group has been the cause of bewilderment and despair to generations of medical students. Many names, such as those of Gull and Sutton and of Weigert, might be quoted amongst the pioneers who exposed the futility of this classification; their voices were unfortunately not heard, although the rapid growth of histological inquiry soon made it apparent to the pathologist that there was no justification for the acceptance of it.

The first decade of the present century saw the genesis of a 'functional' classification of nephritis which originated in France following the revival of biochemical investigation, chiefly as the result of the observation of Vidal and his school. This school sought to divide Bright's disease into a group of patients in whom the damaged kidney was unable to excrete nitrogenous substances and hence produced uræmia, with, in opposition to this, a group in which the disease produced failure to excrete chlorides and other salts and hence produced œdema. At the present time it is unnecessary to say very much concerning this classification beyond that it had a transient value in focusing attention on biochemistry, and that the course of time has amply demonstrated not only that many patients could be placed in both groups simultaneously, but that modern biochemistry has rejected the theory that there is a type of kidney essentially incapable of excreting chloride.

To-day we are approaching a classification which has a sound basis of morbid anatomy and is also compatible with the various clinical manifestations of nephritis. Admitting that the widespread body of observers to whom I referred in the opening paragraphs of this paper has not yet reached agreement as to details, it is becoming more and more generally recognized that three great groups are to be distinguished. Of these the central group is constituted by the true inflammatory diseases of the kidney following acute infections. This great group of glomerulo-nephritis may be subdivided into a relatively benign group in which scattered foci of inflammation arise during an acute infection, and a second group in which the inflammation is spread diffusely through both kidneys. This latter subgroup includes all those serious cases of nephritis which, beginning usually as a streptococcal infection, are seen again and again in the medical wards of the general hospitals, and eventually terminate fatally, usually after a very chronic course. In very severe cases the initial effect may be so tremendous as to produce renal failure and death from uræmia. More often an œdema of gradual onset is accompanied by a slowly rising blood pressure, and after waxing and waning for long periods tends to subside as renal failure slowly appears. Death will occur from true uræmia or from cerebral hæmorrhage or from pseudo-uræmia, according as the factor of glomerular destruction or of increasing hypertension is predominant.

Now in sharp opposition to this great group we recognize two other groups which have little if anything in common either with one another or with true inflammatory nephritis. The first of these is that which has

been called 'nephrosis'. Here we have, clinically, an intense albuminuria, with or without œdema, but without either marked hæmaturia, increase in blood pressure, changes in the retina, or any tendency to uræmia. On the histological side we recognize the association of this group with kidneys showing no evidence of change in the glomerulus, but changes, purely degenerative in character, in the renal tubules. The recognition of this group is due largely to the work of Epstein, and if at the present day there is a tendency to reject his belief in the invariably benign character of nephrosis, it remains true that the prognosis in many examples is relatively good. Perhaps the most important lesson from his work has been that whereas even five years ago there was a tendency to say that 'renal œdema was an entirely mysterious phenomenon, it is now becoming agreed in all quarters that diminution of the density and osmotic capacity of the blood-plasma, following leakage of albumin into the urine, is the mechanical factor responsible for the production of renal dropsy. Examples of nephrosis are to be found in cases where the kidney has been damaged by the accidental or suicidal administration of mercurial poisons; another group is that known as lardaceous disease; but many cases have been reported arising apparently spontaneously. The great difficulty concerning nephrosis is that a certain number of these latter cases are found, with the passage of time, to develop hypertension and renal failure. These are examples which probably have been mistakenly diagnosed at the outset, being really cases of diffuse glomerulo-nephritis in which the initial glomerular damage was so slight as to escape recognition.

At the further extremity of the scale we find another main variety, contrasting vividly with nephrosis and constituting the third of the great main groups of renal disease. This is the division which includes all those cases in which the kidneys are damaged by changes in their blood-supply following some generalized vascular degeneration. Perhaps the best name to give to this group is 'ischaemic nephritis'. The outstanding clinical manifestation of these is hypertension, the outstanding feature of their morbid anatomy is sclerosis of the kidneys and spleen, with hypertrophy of the heart. Several subdivisions of this group are becoming recognized, but I do not wish to complicate the story by entering into fuller description of these beyond saying that far and away the most frequent cause of ischaemic nephritis is that mysterious condition which we speak about as 'essential hypertension' or 'hyperpiesia'. I cannot too forcibly remind you that death in this group arises far more frequently from cerebral catastrophe or from cardiac failure than from renal failure; many authorities have stated their conviction that less than 10 per cent of all such patients die of uræmia and renal failure, but many pathologists, finding in the post-mortem room a body with conspicuously shrivelled kidneys, incline even to-day to group all such cases as 'chronic interstitial nephritis'. Very brief histological examination of other organs, such as the spleen, should be sufficient to demonstrate that to regard such cases as primary diseases of the kidney is to fall into grave error. Sir William Gull, many years ago, had occasion to question the conception of the great Bright in this respect. Lecturing on some preserved specimens consisting of a large heart and two contracted kidneys, he said that not these alone but the entire man should have been included in the vase.

I do not wish it to be supposed that there are no clinical difficulties as regards the allocation of certain cases to this last group. True inflammatory disease of the kidney may be so insidious in its onset, and may be accompanied by such widespread arterial change, that hypertension is altogether predominant in the picture, but for every case of true chronic nephritis of this type there are probably 50 in which primary arterial disease is mistakenly classed as chronic interstitial nephritis.

Surgical Treatment of Pulmonary Tuberculosis

By E. BELLINGHAM-SMITH
and

ANTHONY FEILING

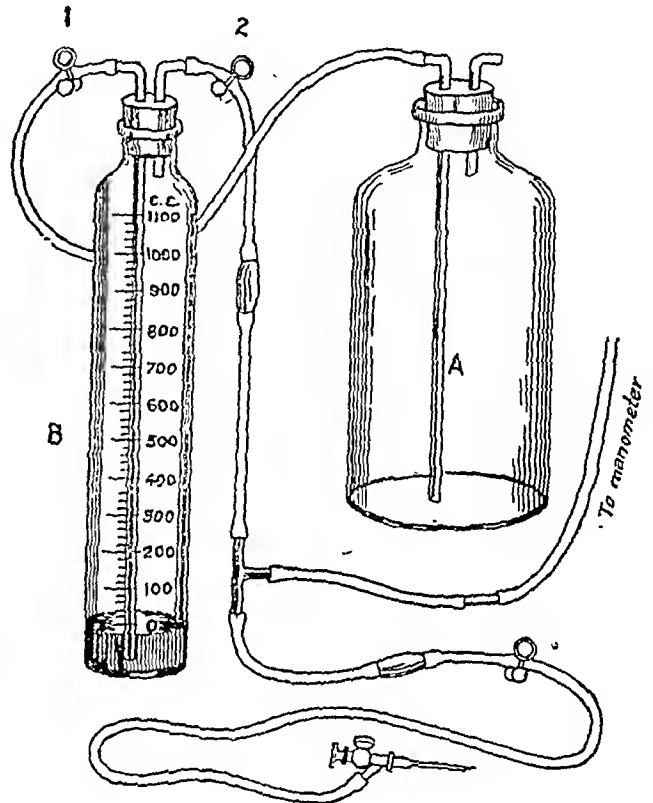
(Abstracted from the *Modern Medical Treatment*, Vol. II, p. 527. London: Cassell and Company, 1931)

THE operative treatment of tuberculosis of the lungs includes the performance of artificial pneumothorax, phrenicotomy and thoracoplasty. In artificial pneumothorax we have an important aid to treatment. In cases where the disease is unilateral but not reacting to rest and treatment and advance is rapid, the application of artificial pneumothorax may cause not only a definite arrest in the disease, but also free the patient from all the symptoms of an acute toxæmia. It is further of value in recurrent and severe hæmoptysis, and may be used in conjunction with sanocrysin where the disease is bilateral. It is not absolutely contra-indicated in cases where the disease in the opposite lung is slight. This method of treatment has been further adapted so that a partial pneumothorax has been instituted on both sides in cases of bilateral disease, there being some evidence to show that the gas so introduced tends to collect over the affected area and cause a local compression. The immediate results of the operation are striking. Fever, cough and sputum cease, the pulse decreases, the appetite improves, weight increases and the sallow, hectic appearance associated with toxæmia is replaced by a healthy colour. The ultimate results are not perhaps so easy to determine. Pleurisy with effusion occurs in 40 to 50 per cent of cases, permanent collapse occurs in a limited number, while in others a degree of expansion may occur associated with some resumption of lung function. In still others the expansion takes place with diffuse fibrotic and bronchiectatic changes and adherence of lung to the chest-wall. The dangers of this operation are: (1) pleural shock; (2) penetration of lung, and gas embolism; (3) injury to lung or tearing of adhesions giving rise to a pyopneumothorax, and (4) a rapid extension of the disease in the contralateral lung from overwork induced by the collapse and loss of the unhealthy one.

For the induction of an artificial pneumothorax there are several types of instruments, all based on the same principle. Those in common use are Forlanini's and Lillingston and Pearson's (see diagram). But it is possible by a little ingenuity to improvise one. All that is required is two glass jars, one graduated in cubic centimetres, and a U-shaped manometer fixed on a scale graduated also in cubic centimetres and recording positive and negative pressures. A three-way glass connection, some rubber and glass tubing, three metal clamps, a quantity of sterile wool, some mercuric perchloride solution for the bottles, and a coloured liquid suitable as an indicator for the manometer, complete the requirements. The whole, when fitted together, can be carried in a wooden case. Two needles are usually advised, one for the primary induction and one for the refills; the first is a trocar and cannula with blunt but cutting edge, the second has the pointed bevelled extremity of an ordinary exploring needle. Both have a tap and by-pass tube in the hilt. It will be seen from the diagram that when the needle is in the chest, release of clamp 3 places the pleural cavity in contact with the manometer. At the same time the respiratory movements will be registered by an oscillation of the column of fluid. With the release of clamps 1 and 2 the wash-bottles A and B are introduced into the circuit, and elevation of A will force air out of B into the chest cavity. The quantity of air so transferred is measured by means of the graduations of B.

Before the operation is begun the whole apparatus should be carefully sterilized and examined for leakage,

and the tubing, filters and needle should be thoroughly dried. For induction the patient should be in bed, a preliminary dose of omopon or morphia being given to allay nervous excitability. He lies supine, but turned somewhat on to his sound side so as to bring the site of operation directly uppermost, the head being low in order to reduce the risk of gas embolism. The arm is removed from the sphere of action by stretching it above the head, and letting the hand grasp the bed-rail behind. The usual site for puncture is the sixth space in the anterior or mid-axillary line, for this is shown to be the site most free from adhesions, and also where the lungs show the most marked respiratory excursions. The skin is cleansed, and sterile towels are placed round the area of operation. Novocain is injected slowly into the skin and deeper tissues down to the pleural layer, so as to guard against pleural shock. The needle is



now introduced carefully and gently through the chest-wall as far as the pleura. The trocar of the needle is withdrawn, the tap on the hilt is turned and clamp 3 is released, placing the needle in direct communication with the manometer. The cannula is now pushed through the pleura into the pleural cavity. When the cannula has entered the pleural cavity a negative pressure will be recorded on the manometer and oscillations of the column of fluid through a range of 3 to 10 cm. will be seen corresponding with the respiratory movement. Before the needle enters the pleural cavity care should be taken to warn the patient against coughing. If oscillations do not occur after the needle has supposedly entered the pleural cavity either the needle has not penetrated the parietal pleura, or the lumen is blocked, or the lung has been penetrated.

Introduction into or injury to a vessel will be shown by a positive pressure, or by the presence of blood in the glass connection between the needle and the manometer. If air is admitted before the needle has entered the pleural cavity, surgical emphysema will result, or if it is admitted after the introduction of the needle into a pulmonary vessel gas embolism and sudden death may occur. It is therefore important to be certain that definite oscillations of a negative type are occurring, corresponding to inspiration and expiration, before air is admitted. The introduction of the air is accomplished by releasing the clamps 1 and 2 between the wash-bottles in series and the manometer

and needle in the chest. Air is drawn into the chest from the second bottle B and fluid passes from the first bottle A into bottle B to replace it. By gradually raising bottle A, further air can be introduced. A convenient amount of gas for the first operation is 200 to 300 c.c., but, even so, the essential factor is the manometer reading. If the gas flows in easily and the patient complains of no increasing discomfort this amount can be run in, with the pleural pressure still remaining on the negative side; a lung can be adequately collapsed with the pleural pressure never exceeding 2 c.c. of water. If, however, the pleural space is not free, the introduction of only a small amount of gas will show a manometer reading on the positive side, and may be accompanied by a certain amount of pain and distress. The needle is then withdrawn and the puncture covered with iodine or collodion. Refills will be required two days later and again in three days after the second refill. Thereafter, refills will take place at longer intervals—one week, ten days, fourteen days, twenty-eight days; the time will vary with the degree of collapse secured with the condition of the patient and his reaction to the treatment, and with the rapidity of absorption of gas, which varies very materially with different individuals.

Over-pressure will cause discomfort and dangerous displacement of the mediastinum. On the other hand, a failure to maintain sufficient pressure, with consequent re-expansion of the lung, defeats the object of the operation, and will terminate in the rapid formation of adhesions and compulsory abandonment of the artificial pneumothorax. The degree of collapse can be controlled by careful x-ray observation. During the first few weeks of induction the patient should be at rest; afterwards refills may be undertaken, and the patient need only rest for a few hours following the operation.

Artificial pneumothorax, though indicated by the stage or character of the disease, is not always feasible on account of adhesions between the visceral and parietal pleurae. In some of these cases where adhesion is not dense, division of the adhesion may be undertaken by cautery, access to the chest and localization of the adhesions being obtained by the thoracoscope. Where the adhesions are mainly basal, a preliminary phrenicotomy may be undertaken. This causes a paralysis of the diaphragm on the same side, enabling the base of the lung to collapse. It has been used by itself as a means of promoting rest in the infected lung in very acute, rapidly progressive lesions where pneumothorax and thoracoplasty, on account of a bilateral infection, were contra-indicated; but it clearly cannot cause that complete collapse and immobility which is provided by artificial pneumothorax, or, as we shall show later, thoracoplasty.

Phrenicotomy, or a more extensive removal of the phrenic nerve, exsiccation, has certain further advantages when performed in association with artificial pneumothorax. There is less likelihood of pleural effusion. The smaller pleural cavity eventually left better accommodates the contracted lung, and there is less liability to reactivation of tubercle in the compressed lung and, when the pneumothorax is discontinued, to re-expansion of cavities which have been previously closed. For when pneumothorax is discontinued almost immediate adherence takes place between the lung and the chest-wall. Such adhesion, in conjunction with the constant contraction set up in the lung itself by the fibrous tissue formed during the collapse period, along with respiratory movement, will tend to stretch the fibrous scar-tissue around areas of tuberculosis and cavitation. There is a further tendency to the formation of bronchiectasis in the remaining healthier lower portions of the lung, which phrenicotomy may prevent, while its further service is shown in correcting the mediastinal displacement which follows partial re-expansion. Where pneumothorax can be successfully maintained the final difficulty lies in knowing when to stop. Reactivation has taken place in certain cases after considerable periods have elapsed.

It would seem wise therefore, when possible, to persist in this treatment for a period of at least two years. Many authorities advocate three to five years.

When for reasons given above, artificial pneumothorax has to be abandoned, or when in the fullness of time it is discontinued and reactivation occurs, or bronchiectasis or chronic empyema makes life unbearable, there arises the question of thoracoplasty. This operation has for its purpose the same object as artificial pneumothorax, viz, the compression and putting at complete rest of the diseased lung. The indications for its performance are suggested above, and the conditions under which it is carried out are the same as those for phrenicotomy and artificial pneumothorax, namely, advanced pulmonary tuberculosis in one lung with little or no infection in the other lung. It may be undertaken alone as a paravertebral thoracoplasty of ribs 1–11, or as a partial resection of ribs 1–7 with radical phrenicotomy. As a rule, phrenicotomy is preferably performed before either the complete or partial operation. The operation itself consists in the extra-pleural resection of 1 to 6 inches of each of the first eleven ribs. This is carried out in either one or two stages. Its effect is to produce a collapse of the chest-wall, with rigid fixation and a complete and permanent shrinkage and compression of the diseased lung. The immediate mortality from this operation is less than 2 per cent, the delayed mortality from causes indirectly concerned with the operation about 13 per cent. When one considers that the type of case required for this operation is usually advanced and the eventual prospect hopeless, such a mortality does not appear to be excessive. Alexander, in his book *The Surgery of Pulmonary Tuberculosis*, analyses 1,159 cases operated upon in the last seven years. Of these, 36.8 per cent were completely cured or clinically cured, 24 per cent improved, 5 per cent were living but unimproved, and 33 per cent had died. It is early to claim a permanent cure for the cases reported as cured, but the degree of success attained was a remarkable achievement in view of the hopeless character of the stage at which the disease had arrived.

Influenza

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SIGNS AND SYMPTOMS

THE story of onset given by the majority of patients is surprisingly similar, and runs as follows: First of all a feeling of weariness, followed by dryness or soreness of the throat. In four to five hours this is added to by an aching in the limbs; the arms feel heavy; the legs ache, and the effort of taking a deep breath or of coughing causes a pain beneath the shoulder blade, or round the lower ribs. This is often accompanied by a feeling of constriction round the head, followed by throbbing in the temples, and a pain running up behind the jaw into the post-aural region. Intense weariness and disinclination for effort become evident, and then suddenly the patient feels hot and flushed, perspiration seems imminent, but instead a cold frozen feeling, a shivering attack, or a rigor supervenes. Three or four of these may follow each other at short intervals. It is usually about this time that the patient retires to bed and the doctor is called in. On examination the patient looks somewhat anxious, with furrowed brows, slight photophobia, and is disinclined to read. Most patients are limp and lethargic, and quite content to curl up. The body pains tend to increase, and shift about from place to place—arm, shoulder, calf, hip, etc.—but frequently settle finally in the loins and lower rib region. The temperature is not considerably raised, in the majority of cases being about 101°–102°F. A few

endeavouring to lower the patient's temperature by salicylates or aspirin, though the latter may be given with caution to ease the headache or body pains. Frequent mouth washes with potassium permanganate (1:4,000), and trochiscus potassii chloratis, gr. 5, four-hourly, are useful, with a view to limiting the multiplication of pyogenic organisms always present in the mouth and nasopharynx. Local applications to the upper part of the chest and neck in the form of poultices and liniments are useful for allaying the cough and substernal uneasiness. Tinctura benzoini composita (four parts) with menthol or eucalyptus (one part), as an inhalation, with the administration of tinctura camphoræ composita, may be useful in the treatment of a very irritable cough. The latter should never be used where there is any implication of the smaller bronchial tubes, with or without cyanosis, and the former avoided in the severer types of influenzal laryngitis and tracheitis where there is dyspnoea from swelling of the mucous membrane of the glottis, for œdema of the glottis can develop.

BRONCHITIS (DIFFUSE BRONCHITIS, LOCALIZED BRONCHITIS, SEVERE PURULENT BRONCHITIS)

With the destruction of the ciliated epithelium of the larynx and trachea, these are laid open to invasion by streptococci and pneumococci, and other inhabitants of the upper respiratory passages. This may result in a spread of inflammatory processes down the main and smaller bronchi, and the clinical picture of diffuse bronchitis.

In the earlier stages of the bronchial affection the cough is dry, and expectoration scanty and viscid. If the smaller bronchi are involved the cough becomes more distressing, and may be paroxysmal. Dyspnoea may be a troublesome feature, and cyanosis marked; this being due to swelling of the mucous membrane and accumulation of debris in the tubes. This swelling and exudation in some influenzal epidemics has been so extensive and severe as to largely occlude even the main bronchi. After a few days the sputum becomes more abundant and mucopurulent, and in the severer cases may contain blood. At this stage, with no further extension of the inflammatory process, the dyspnoea and subjective tightness of the chest become relieved, but the expectoration and cough may continue with diminishing severity for several weeks.

With only the larger bronchial tubes involved there will be no objective signs, but it is more common to have more extensive involvement of the smaller bronchi with dry râles throughout the lungs though more marked at the bases. With resolution of the bronchitis these râles become coarser and moister, and clear up in a few days or so. With extension of the inflammation, these râles become finer and stickier, and approach in character to crepitations—crepitant râles: this signifies the onset of capillary bronchitis or bronchiolitis.

It may be expedient to mention here that influenza can be complicated by a localized bronchitis. Of course, localized bronchitis is usually symptomatic—at the apex of tuberculosis, at the base of hypostatic congestion. It is wise even in the localized bronchitis of influenza to have in mind an area of pulmonary tissue of inferior resistance, the potential seat of tuberculosis, or even its present nidus flamed into activity by the catarrhal process. The onset of pulmonary tuberculosis has often been associated with, and even ascribed to, an attack of influenza.

With this diffuse bronchitis, alkalis in the early stages and stimulating expectorants later both have their place in aiding the expulsion of infected material from the lung. Tinctura benzoini composita inhalations are useful in selected cases, with no more than a little respiratory embarrassment. Counter-irritants to the chest give subjective relief to the sense of constriction and tightness in many cases. Oxygen will relieve the respiratory distress associated with cyanosis in those cases in which this is not due to further extension of the morbid process leading to exudation into the pulmonary alveoli.

It has been the common experience in the recent epidemic of influenza complicated by bronchitis, for cough to persist for weeks after the patient is up and about. This is due to the slow recovery of the bronchial mucous membrane, which is always so severely damaged in these cases. Especial care is needed in the convalescence of influenzal bronchitis for this reason, and I always advise that the patient be confined to an even temperature for a week at least after the disappearance of all signs from the chest.

CAPILLARY BRONCHITIS, BRONCHO-PNEUMONIA AND HELIOTROPE PNEUMONIA

When the smallest bronchi and bronchioles become inflamed, the terminal alveoli almost invariably become involved, for little swelling of the bronchiolar wall is sufficient to occlude the lumen of the tube with the production of an area of lobular collapse. The inflammatory process then extends into some or all of these areas, and broncho-pneumonic consolidation results.

Clinically the implication of the finer tubes and alveoli is signified by a further rise in temperature, greater difficulty with respiration, often associated with a marked degree of cyanosis, and an irritating shallow and persistent cough. The earliest findings on examination are the presence of crepitations in contrast to the bronchitic râles of the former stage. They appear often as an inspiratory burst of abundant fine and rather consonating, moist sounds. The lobular consolidation which goes hand in hand with the bronchiolitis may give rise to no further signs, and as such has to be presumed, as the autopsy table so often shows. Compensatory emphysema may be more than sufficient to overcome the dullness which otherwise would be elicited, and, indeed, a hyper-resonant note is not uncommon. It is common to find different signs simultaneously in various parts of the thorax, sometimes on one side, sometimes on the other, and they may alternate with one another in the protracted forms.

Of course, the degree of severity of this condition varies, on the one hand, with a few scattered areas of bronchiolitis and broncho-pneumonia with rapid resolution, and, on the other, with a progressive diffuse inflammation associated with a dyspnoea so violent that the patient suffocates. This is sometimes called suffocative catarrh; it is in its acutest form characterized by extreme prostration and a heliotrope tint of the skin and mucous membranes, usually followed by death in from twelve to twenty-four hours in spite of all forms of treatment—the so-called 'heliotrope pneumonia'.

Therapeutic efforts must be directed chiefly to sustaining the patient's strength and combating the toxæmia and circulatory failure. In regard to the first of these, good and efficient nursing can never be overstressed. An easily digested food with carbohydrate should be given in small quantities and frequently. Alcohol is useful, and should be pushed to its physiological limit. When the lungs are rapidly filling with serum and mucus a dose of atropin sulphate (gr. 1/75) will often arrest the secretion, and tide the patient over a critical period; stimulating expectorants have also their place in the stage of free secretion. Narcotics may have to be resorted to—rest is all-important—but any form of opium should be strictly avoided. No drug should be given unless there is a clear necessity for its use—they can help the patient, but they cannot cure him.

BRONCHIECTASIS, BRONCHIOLITIS FIBROSA OBLITERANS, ABSCESS AND GANGRENE

The bronchioles lack the protective loops of cartilage of the bronchi, and when they have been involved in a severe inflammatory process their muscular wall undergoes in places degeneration and atrophy and the resultant weakening of their walls is followed by dilatation and bronchiectasis.

Bronchiectasis is more liable to develop in those cases in which the sputum has been particularly purulent and foetid, and in those in which the bronchiolitis has run a protracted course.

Sometimes, but rarely, organization of the bronchiolar and pneumonic exudate takes place by a fibroblastic proliferation from the alveolar and bronchiolar walls, leading to a patchy but severe fibrosis of the lung. Pathologically, this condition is known as bronchiolitis fibrosa obliterans; clinically, it is included under the generic term—unresolved pneumonia. It necessarily results in the ultimate loss of function of whole groups of alveoli, and is liable to be followed by persistent dyspnoea and cyanosis. It tends to occur in the more debilitated patient and in those in whom the bronchiolitis has persisted for an unduly long time.

Multiple small pulmonary abscesses and areas of gangrene are not uncommon in the severer types of broncho-pneumonia complicating influenza, but death supervenes in the broncho-pneumonic stage. A solitary large suppurative focus or pulmonary abscess is extremely rare, and should be suspected when, after the resolution of the general broncho-pneumonic process, symptoms of localized pus formation, and perhaps with signs of an area of pulmonary consolidation, persist. Clubbing of the fingers can occur very early in cases of lung abscess.

LOBAR PNEUMONIA AND INFLUENZA

Lobar pneumonia is not usually regarded as a manifestation of influenza, and when compared with the incidence of broncho-pneumonia it is negligible; but I have seen a case recently in which it suddenly developed during the convalescent stage of a mild influenzal bronchitis.

PLEURISY, PLEURAL EFFUSION AND EMPYEMA

Pleurisy occurs sometimes quite early on in the respiratory type of influenza. It means that pyogenic organisms have gained entrance to the bronchial lymphatics, and have spread down through the lymphatics of the pulmonary parenchyma to the visceral pleura of the lung. The common signs of pleurisy are found usually associated with pain; effusion may follow.

Effusion is more likely to follow in those cases in which pleural inflammation has occurred over areas of broncho-pneumonic consolidation in the lung. In some cases it is most important to realize that the bronchitis and patchy broncho-pneumonia are quite insignificant, and an empyema insidiously develops and becomes the chief factor in the disease. In other words, pleural effusion may develop and become purulent when consolidation in the lung has been minimal, and has escaped the notice of the medical man in attendance.

The presence of fluid in the pleural sac is suggested by a persistence of the patient's temperature, with resolution of the inflammatory process in the lung. The more useful sign is the development of a duller note usually at one base or the other, with feeble or absent breath sounds over this dull area. Repeated careful exploratory punctures are advisable where the signs and symptoms would suggest the presence of fluid in the pleural space.

In contradistinction to the empyema fluid aspirated in lobar pneumonia, which is usually frank pus at the time of the first puncture and contains many organisms (pneumococci), the effusion in influenza is often of a sero-fibrinous nature, or slightly opalescent. A few organisms may be found in smears from the fluid, but cultures from the same fluid may be sterile. The streptococcus, pneumococcus, and less often the influenza bacillus, are commonly found. These effusions may become purulent, but, on the other hand, can absorb and clear up sometimes with repeated puncture. An empyema operation is inadvisable until the fluid is obviously purulent, and until this occurs repeated pleural puncture may be necessary in large effusions to relieve any respiratory distress, and in the smaller effusions may obviate the necessity for rib resection altogether.

In this short article I have tried to indicate that the primary lesion at the root of the whole matter in influenza is a naso-pharyngeal catarrh and tracheo-bronchitis, which allows other organisms an easy access

to the pulmonary tissue. In the dreaded pandemic cases the virus increased in virulence results in a hæmorrhagic œdema of the lung with a blood-stained, watery fluid pouring out of the bronchi, much as it did in the first cases of gas poisoning in those early days at Ypres; no known treatment in these cases is of any avail. I have attempted to show in the complications following the tracheo-bronchitis that through their whole course there is a simple basic theme which is played upon and altered by the different secondary invading organisms, and the variable resistance of each patient. I have dealt as far as possible with the inflammations in the lung that become chronic, and would stress again the often peculiar insidious development of empyema.

A realization of the course that the influenzal pulmonary state may take, and the common course that it does take, will lead us to preventive measures at different stages, and treatment on more rational lines at the inception of each stage.

The Prevention of Colds and Other Respiratory Infections

By DAVID THOMSON

and

ROBERT THOMSON

(Abstracted from 'The Common Cold', the *Annals of the Pickett-Thomson Research Laboratory*, Vol. VIII, December 1932, p. 657)

THE various methods used for the prevention of colds may be briefly enumerated as follows:

(a) *Measures which reduce the chances of infection.*—These are the avoidance of crowded places during epidemics, avoidance of patients and sick-rooms, avoidance of dust-laden atmospheres, and avoidance of kissing. The chances of infection can also be reduced; not so much by trying to avoid it, but by measures which insure better ventilation of public places of amusement, of schoolrooms, of factories, offices, and of school dormitories. Coupled with better ventilation we must have more space so that the individuals are less crowded whether in the schoolroom, the dormitory, or the factory. This provision of more space reduces the chance of droplet infection.

Other measures which reduce the chances of infection are the sterilization of the air by formalin vapour, etc.; sterilization of fomites, towels, handkerchiefs, etc.; the wearing of masks by the patients, isolation of patients, and the exclusion of carriers.

Probably one of the most important methods of reducing the chance of infection is by means of gargling the throat and treating the nasal passages with some mild antiseptic once or more times daily, more especially during epidemics. There has been a great deal of controversy over this procedure, but it seems to us extremely reasonable to suppose that just as we can prevent infection with venereal diseases through the application of antiseptics soon after exposure so should we be able to prevent droplet infection from respiratory diseases by gargling and washing out the nasal cavities with weak antiseptics.

No one objects to gargling, but the practice of nasal douching has been strongly condemned by many nose specialists because of the danger of thereby causing infection of the nasal sinuses and the middle ear. There can be no doubt that nasal douching by means of forceful injection as with a Higginson syringe is dangerous and should never be done. All such dangers, however, are avoided if we sniff the antiseptic lotion up the nose, because this sniffing produces a negative pressure and avoids the danger of forcing septic material into the sinuses or into the Eustachian tubes. The other danger is the use of too strong antiseptics because these damage the delicate mucous membranes and render them more liable to infection than before. If, however, we use extremely weak and non-irritating antiseptics and sniff them up the nose, we consider that this, combined with gargling, is very good practice if carried out night or

morning or soon after any exposure to infection; more especially during the prevalence of epidemics.

(b) *Measures which increase resistance to catarrhal infections.*—Probably the most important of such measures is the remedying of inherent defects in the nose, such as the removal of polypi, adenoids, and other unhealthy obstructions. The removal of obviously diseased tonsils is also important. There has been some opposition in recent years to the wholesale removal of tonsils and adenoids such as has been practised for some years past, but in our opinion this is only the swing of the pendulum to the opposite extreme due to the fact that it has been overdone in the past. We think that there can be no doubt that grossly enlarged and unhealthy tonsils and adenoids should be removed. There has also been too much tendency to operate on the nose, but if moderation and discretion is used in this matter there is little doubt that the patient will derive great benefit from the surgical treatment of gross defects in the majority of instances.

(c) *Dietetic methods of increasing resistance.*—There can be no doubt that proper feeding increases the general resistance to disease. No definite rules, however, can be laid down for every person. Some individuals eat too much and others eat too little. In general, one would recommend a well-balanced diet with a sufficiency of vitamins. Rickety children are susceptible to colds, so a sufficiency of vitamins A and D are essential. Cod-liver oil was formerly administered for this purpose, but there are now many substitutes and vitamin extracts on the market.

(d) *Avoidance of constipation.*—We believe that the general health, and therefore the bodily resistance, can be greatly improved by keeping the bowels cleared out two to three times a day. The importance of this is not fully realized either by the medical profession or by the public. The best way to keep the intestine clean is to clear it out several times a day. This is vastly superior to the use of so-called intestinal antiseptics. Some medical men seem to think that purgatives are to be avoided. In our opinion they should be used continuously by many individuals, and the dosage does not require to be increased if the type of laxative is changed or varied from time to time. We know a very healthy and active old lady in Scotland, aged 98, who has used powerful purgatives more or less constantly for a period of more than 50 years. Her son, who is a doctor, aged 60, had constantly warned her for many years on the dangers of purgative medicines, but she refused to take his advice, and now this doctor himself is a convert and a firm believer in his mother's teaching in this respect. In these days of overeating and sedentary living it is sound common sense to clear the bowels out thoroughly at least twice a day, and there are innumerable excellent laxatives for this purpose.

(e) *Ultra-violet light.*—We believe that ultra-violet radiation is an excellent thing during the long, sunless winter months, and that this is an aid in increasing our resistance to colds.

(f) *The importance of warmth.*—We have seen that chill and any drop in the temperature of the atmosphere predisposes to colds. It is sound common sense, therefore, to keep ourselves adequately warm during cold weather by means of a sufficient amount of clothing and by sufficient warming of the houses and rooms in which we work. Those who advocate that we should go about shivering with the idea that we are hardening ourselves, and that this is correct because some savages do so, are not level-headed, but should be regarded as cranks. Their advice is quite wrong for the average sedentary worker.

(g) *General hygiene, exercise, fresh air, baths, etc.,* are all to be strongly recommended, provided that discretion is used, and so long as it is remembered that it is possible to be over-enthusiastic and to overdo things. Violent exercise after middle age or too prolonged exertion will do harm, and cold baths do not suit many people. On the other hand, very many people

living in towns take far too little exercise and become exceedingly flabby. The most important muscles in the body to exercise are the abdominal muscles. It is far more important for health that the abdominal muscles should be strong and firm than that the biceps should be developed.

(h) *The importance of the early eradication of all septic foci.*—We have now finished our eighth volume of these Annals, and in the course of our studies we have consulted about 15,000 research papers. In pondering over this enormous mass of medical research, it seems to us that the most important fact which stands out above all others is the danger and far-reaching effects of septic foci in any part of the body. Any septic focus on the skin is immediately seen by the patient and as a rule is attended to at once. When, however, similar small septic areas occur around the teeth, or at the apices of the teeth, or in the throat or tonsils, or in the nose, or in the intestine, they are not as a rule noticed, and remain unattended. Nevertheless, it is these small initial spots of sepsis which spread and lead to systemic infection. They are the beginnings of long-continued chronic illness and the cause of premature decay and death. A tiny focus of sepsis no bigger than a split pea around or at the apex of a tooth may start a long-continued and persistent fibrositis in some distant part of the body. Similar septic foci in the gums and mouth may set up repeated attacks of tonsillitis and catarrhs of the respiratory tract. It is in these small septic foci that the bacteria of respiratory catarrh lurk, and they are ever ready to spread rapidly from these unhealthy areas when the resistance of the body is lowered. We have already pointed out at length the far-reaching dangers of sepsis in the nasal sinuses, and have shown that these septic foci, which are most persistent if not attended to, cause repeated reinfections of the whole respiratory tract leading even to bronchitis and bronchiectasis. The situation will be more easily grasped if we think of an ordinary tree. The average tree as a rule dies of rot, and that rot commences as a small area usually due to an injury to the bark. This gradually spreads if unattended to, and after the course of years causes the final death of the tree. This same and simple truth applies equally to the human body, and we cannot urge too strongly upon medical men and upon the general public the importance of searching for and eradicating at once all small foci of sepsis or suppuration in any part of the body. The most common site for these is in the mouth and around the teeth. Great advances have been made in detecting septic foci about the teeth by means of x-rays, and full advantage should be taken of this at frequent intervals or at any rate at least once a year. Of equal importance is the radiological examination of the sinuses of the nose. Much human suffering and disease could be avoided by such intelligence and foresight, and the healthy constitution to which we aspire could be prolonged for a much greater time. Above all, remember that cleanliness and the diligent eradication of small septic foci in the mouth, teeth, and nose are even more important for health than the much lauded importance of fresh air, exercise, and bathing of the outside of the body.

(i) *The importance of cleanliness in the prevention of colds.*—We have seen that colds are caused by certain species of pathogenic bacteria. The greatest enemy of all pathogenic bacteria is cleanliness and hygiene in its widest sense. We have already pointed out the great importance of cleanliness and hygiene with regard to our bodies.

The importance of bathing so as to keep the skin clean has long been preached, but we have pointed out the still greater importance of scrupulous care and cleanliness with regard to the hidden and unseen recesses of the body, namely, in the mouth, nose, and elsewhere.

Equally important is the hygiene and cleanliness of our clothing and of the various objects which we use in daily life. Just as important also is the hygiene of our surroundings; thus scrupulous cleanliness is required

in the home, in the school, the factory, the office, the shop, the bus, the theatre, etc., etc. This cleanliness requires ample ventilation, frequent washing and extraction of dust.

Dust is an important factor in the causation of colds. The principal cause of dust in the streets of London is the excrement of horses and dogs. It seems to us that the London County Council and other town councils should do something active about this matter. It is just as important as the problem of pollution of the atmosphere with smoke. People who keep dogs in cities should be compelled to provide special water-closets for them in their own houses. Horses should now be disallowed in all large cities, for not only are they the chief cause of pollution of the streets, but they interfere very greatly with the normal motor traffic.

The keeping of domestic animals, such as dogs and cats, is a problem which requires very much investigation. So far we know nothing with regard to the part played by animals in the genesis and spread

of epidemics of colds. Hoyle's recent work, which clearly shows that mice are highly susceptible to several of the bacteria which cause colds in man, is very significant. Highly susceptible animals are apt to pass these bacteria back to man in a much greater state of virulence. Who knows, therefore, whether or not the pneumococci are coming back to us from mice through the agency of cats?

It is important, therefore, that all houses should be constructed so as to be vermin-proof, and it is important that our domestic animals should be kept as clean and as healthy as ourselves. Animals of the rodent type are of enormous importance in the spread of plague; they may be of equal importance in the spread of the common cold. We have found streptococci and Gram-negative cocci of the catarrhalis group in fleas which have been fed on rats. Serious investigations are required into all these matters, more especially as the common cold is one of the greatest scourges of civilization in the temperate climates.

Reviews

THE MEDICAL ANNUAL: A YEAR BOOK OF TREATMENT AND PRACTITIONERS' INDEX.—Edited by C. F. Coombs, M.D., F.R.C.P. (the late), and A. R. Short, M.D., B.S., B.Sc., F.R.C.S. Fifty-first Year. 1933. Bristol: John Wright and Sons Ltd., 1933. Pp. civ plus 628. Illustrated. Price, 20s.

ONE cannot help being re-impressed each year with the vital importance of this publication to the whole medical profession, and therefore, indirectly, to their patients. By subscribing each year to the *Medical Annual* and devoting a few evenings to its study the practitioner who takes in no medical journal is provided with an opportunity of keeping himself up to date; the man who does receive and read a few medical journals will never fail to find something new with which his journals have not dealt; and the specialist who devotes the best part of the year to the study of his particular subject will receive very considerable benefit by reading up the advances that have been made during the year in other branches of medicine and surgery.

The year has not seen any very striking advances, but steady advances have been made in all branches of medical science. Contemporary history is always difficult to write; advances that seem important to-day may to-morrow be shown to have been steps taken in the wrong direction, or may be forgotten in the more rapid advances that follow; nevertheless, it seems possible that 1932 will be remembered for the introduction of the first really successful synthetic substitute for quinine. This is a subject which is of much greater importance to us in the tropics than to those in the country where this book is published, yet it is a matter that has been given considerable prominence. In fact the various advances in tropical medicine, and more particularly the work done in this country, are always dealt with very fully in the *Medical Annual* each year, and this year is no exception.

Anæsthetists have been very much awake this year and a number of papers have been contributed which place the subject of premedication on a sound footing; nambutal appears to be the most favoured drug in Great Britain. Avertin is still probably the most widely employed of the basal anæsthetics and its dangers, particularly by causing respiratory depression, are said to be controlled completely by the use of coramin.

The effect of the stimulus given to the study of anæmia by the introduction of liver treatment some few years ago has not yet worn off, and the advances that have been made are being consolidated. From an economic point of view the introduction of fish liver in the treatment of the anæmias that respond to liver

treatment is an important one, particularly in England and in many parts of India where fish is comparatively cheap.

The 'diathermic knife' is adopting fresh forms each year and extending its scope. There is now a very ingenious, though very expensive, instrument for transurethral prostatectomy. One sees the advantage of this route in the case of the elderly patient, but the instrument must require very expert handling and its use can scarcely extend much beyond the large city hospitals, so that this particular advance will be of no more than academic interest to 99.9 per cent of the readers of the *Medical Annual*. To mention only such matters is to give wrong impression of the utility of the publication; however, if the general practitioner turns over the next page he will find himself back at his own level with two very practical pages on the subject of the treatment of pruritis ani.

Sialography was a closed book to the reviewer until this year, but one sees the possibilities in the method of 'visibilization' of the salivary ducts by the injection of lipiodol into them. This technique cannot be required very often, but one can imagine that the surgeon would obtain invaluable aid from it in a case of salivary fistula.

Another very useful feature—and I am afraid that this must be the last we mention—is the section devoted to new medical and surgical appliances; our readers will recognize a few of these as having appeared in our 'notes' section during the year.

In view of the fact that medical books appear to be getting more and more expensive each year one cannot help being surprised at the extremely reasonable price of this publication; for fifteen rupees, which I suppose will be the price in this country, no better value could possibly be obtained.

MINOR MALADIES AND THEIR TREATMENT.—By L. Williams, M.D. Sixth Edition. London: Baillière, Tindall and Cox, 1933. Pp. xiii plus 420. Price, 10s. 6d.

DR. LEONARD WILLIAMS is *par excellence* the writer for the general practitioner. He was for many years the editor of that very valuable practitioners' journal, the *Medical Press and Circular*, and since his retirement from this post he has contributed regularly to the paper. Many of his articles have been reprinted, almost word for word, in our Current Topics section, so that he needs little introduction to our readers.

In the introduction to one of the earlier editions of this book the author says that when he was first qualified

he knew a great deal about all the diseases that very few of his patients ever seemed to get, but found that he knew practically nothing about the complaints from which they all suffered, and, failing to get any help from textbooks, he determined that, when his experience warranted it, he would write a book for the use of the general practitioner. He has done; and that book has now been reprinted eleven times in English and once in Spanish.

Dr. Leonard Williams is an extremely pleasing writer; his discourse on the social customs that lead to the development of constipation—a discourse which might well be headed 'the constipated rake's progress' or 'the seven ages of constipation' and which should entitle the author to a place in the National Biography beside Williams Hogarth and Shakespeare—may be taken as a good example of his vivid style. But this chapter is of course written mainly for the European, and the author has in this particular chapter fallen into an old trap. In discussing the evil influence of the European pattern of water closet, he banteringly accuses the manufacturers of being the cause of much constipation. If Dr. Williams were to visit a water-closet maker's factory in England he would find a very large selection of 'eastern pattern' closets on which he could do all the crouching that he wanted. Further, if he came to this country and if he could see through brick walls, he would see not only 'savage man perforce adopting the crouching attitude' but Sanskrit scholars, merchant princes, and world-famous scientists also crouching over Doulton 'bathroom requisites' which would not disgrace the most modern marble-tiled bathroom of the Hollywood 'star'. The fact that constipation is very common amongst the 'crouchers' in this country does not of course detract from the force of the writer's argument.

This criticism is entirely irrelevant, but unadulterated praise, which would be the only alternative, makes sickly reading. The book is not primarily written for this country, but the practitioner in India will nevertheless find it an invaluable guide to the treatment of the everyday ailments of his patients, colds, headaches, indigestion, neuralgias, etc., and we have no hesitation in heartily recommending the book.

A SHORTER ORTHOPÆDIC SURGERY.—By R. Brooke, M.S., F.R.C.S. Pp. 150. With 126 illustrations. Bristol: John Wright & Sons, Ltd., 1932. Price, 10s. 6d.

A SHORT summary of a branch of surgery appears to be one of the most difficult of all books to write, to judge from the mixed reception accorded to several recent efforts. It is made more difficult when the author writes for two different classes of readers, as in the present case. Mr. Brooke aims at supplying the masseuses attached to his hospital with an account of the operative and other treatment carried out in his department on the patients who pass to their care after discharge; he also intends the book for the use of house surgeons. For the latter class of reader the book may be found useful, as it gives a good practical account of many orthopædic conditions—some common, some rare—but sadly restricted in scope by the arrangement of the book on anatomical lines, so that the conditions affecting the skeleton as a whole, such as rickets, osteo-myelitis and bone tumours are not mentioned, nor is there any account of the general pathology of tuberculosis of bones and joints, rheumatoid and gonorrhœal arthritis or of such important conditions as anterior poliomyelitis, spastic diplegia and lesions of the peripheral nerves which supply so many cases for the orthopædic surgeon. For the masseuses the style of the book is too difficult, too much knowledge is assumed and some of the subjects dealt with are above their heads. What interest have they for instance in operations for reconstruction of ruptured cruciate ligaments, a rarely performed operation which was surely introduced by Hey Groves and not by Gallie, to whom it is attributed? Grafting the astragalus on

to the upper end of the femur to fill up a defect left by an acute epiphysitis is a curious procedure, of which the masseuse is not likely to see many examples, she will however be required to treat many cases of stiff joints and adherent muscles or tendons, following injuries or inflammatory conditions, and for this she will get no help from this book; even the treatment of simple sprains is not mentioned, and there are only a few lines on the non-operative treatment of osteoarthritis of each joint. On the other hand many of the sections are good and practical, notably those on congenital dislocation of the hip, internal derangements of the knee joint, flat-foot, congenital club-foot, tuberculosis of the spine and plaster-of-Paris technique. The publishers have maintained their usual high standard of production the illustrations being exceedingly good and well-chosen.

W. L. H.

OFFICE SURGERY.—By F. Beekman, M.D. London: J. B. Lippincott Company, 1932. Pp. xxi plus 402, with 94 illustrations. Price, 21s. Obtainable from Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 15-12.

THERE have appeared at various times a number of books on minor surgery; many of these have been excellent, but this does not mean that there was no room for other books on the same subject. The subject was a very suitable one for the 'Everyday Practice Series', and the author appears to be a man of very considerable practical experience who has the imagination to be able to place himself in the position of the inexperienced and to realize what details will be most valuable to him. The title of the book challenges comment, and, although the author professes to have chosen it because he considers that all surgery is major surgery, we feel that this is a quibble, but that the author, having found that all the changes (manual, handbook, textbook, etc.) had already been rung on the minor surgery theme, was faced with the necessity of breaking new ground; his choice is not a happy one for the British reader, as we do not use the word 'office' in the sense that it is used in America.

The book covers the usual range of minor surgical procedures. The descriptions are clear and the diagrams are useful; it is a common mistake on the part of American writers to overdo the illustrations and occupy space by quite superfluous diagrams and photographs; in this instance this criticism cannot be made.

The book will be found very useful by both students and practitioners in this country where dispensaries and surgeries (or offices) are very modestly equipped.

THE PRACTITIONERS LIBRARY OF MEDICINE AND SURGERY. Volume III. Practice of Medicine. New York and London: D. Appleton and Company, 1932. Pp. II plus 1400. Illustrated. [Available from Messrs. Butterworth and Co. (India), Ltd., Calcutta, the sole agents in India.] Price, Rs. 37-8 per volume. (The set is to be completed in twelve volumes and index.)

VOLUME III of the Practitioners Library is a book on general medicine; nervous diseases have, however, not been included as these will be dealt with in a later volume. The writers are either well-known teachers in different universities in the United States or the occupants of important positions in large institutions in that country. A nice balance has been observed in dealing with the various subjects and aetiology, pathology, diagnosis and treatment are each accorded their fair share of space. Generally speaking, the usual practice has been followed in the allotment of space to the various subjects, but the editor has not followed this slavishly, and certain diseases which have been decreasing during recent years are accordingly dealt with more briefly. An example of this is typhoid, a subject which thirty years ago occupied about 10 per cent of a textbook of general medicine; it is dismissed almost summarily in 26 pages. However, reading

through this chapter one finds it difficult to say what has been omitted. More space has been given to allergic diseases, diseases of the endocrine glands, and other diseases which are assuming a greater importance in view of the advances that have been made in recent years.

The tropical diseases section is as satisfactory as one could expect in a book on general medicine. The editor has been fortunate in getting Professor Hegner to write on most of the diseases that come under this heading, so that, where he has been allowed the space, full justice has been done to the subject, but some diseases, especially those which do not occur in the United States, have been treated somewhat parsimoniously; leishmaniasis is only allowed one very small paragraph. In certain instances there might have been a better liaison between editor and the contributor; for example, we do not believe that Professor Hegner could spread himself on the subject of ascariasis only to the extent of three-quarters of a page; he might with advantage have written another page on the subject, and thereby filled the page which is now blank without adding to the bulk of the book. However this volume maintains the high standard of the series.

We have been requested to state that Messrs. Butterworth and Company will be pleased to supply this complete work on the instalment system, full particulars of which may be obtained from them on request.

PRINCIPLES AND PRACTICE OF OBSTETRICS.—By Professor Joseph B. DeLee, A.M., M.D. Sixth Edition. Thoroughly Revised. Philadelphia and London: W. B. Saunders Company, Ltd., 1933. Pp. xvi plus 1165 pages, with 1,221 illustrations, some in colours. Price, 60s.

The fifth edition of this book on obstetrics maintains the high standard of the previous edition. The general plan is as before; part I is devoted to the physiology of pregnancy, labour and the puerperium, part II to the pathology of pregnancy and labour, and part III to operative obstetrics.

The work is designed, as the author says in the preface, to supply the needs of the student and at the same time provide a wealth of instructive detail and illustrations for the practitioner making an ever-present help in trouble. In this, the author has succeeded and is to be congratulated on the production and the very thorough revision of this monumental work, which contains all the very latest accomplishments in obstetrics. We can commend this book to those who prefer a large treatise, but it will probably appeal more to the qualified man than to the undergraduate.

C. L.

THE COMMON CAUSES OF CHRONIC INDIGESTION: DIFFERENTIAL DIAGNOSIS AND TREATMENT.—By T. C. Hunt, B.A., D.M. (Oxon.), M.R.C.P. (Lond.). London: Baillière, Tindall and Cox, 1933. Pp. vii plus 341, with 16 plates. Price, 12s. 6d.

This small volume has the appearance of a modern novel, being bound and printed in a similar form and it is also of approximately the same length.

The subject of the book 'chronic indigestion' is such a wide one and as the symptoms appear in practically every disease of the stomach a more accurate title would be 'diseases of the stomach'. It is a useful résumé of stomach diseases and quite up to date and as such might be read with profit by any general practitioner, but it hardly appears worth the 12s. 6d. asked for it especially as the information provided will all be found in any recent edition of a standard book on general medicine. There are several good x-ray plates showing bismuth meal appearances in certain conditions.

Numerous references are scattered throughout the book and a long bibliography is appended. This will be no doubt of value to a reader in close touch with large libraries, but a book of this type will probably not appeal to such a man, whereas to the isolated

practitioner who is a much more likely purchaser these references can only be irritating as he is unable to consult the papers and books cited. Their only advantage can be that they show the author has taken considerable pains in presenting his subject as fairly as possible.

This book is one of the 'Minor Monograph Series' of which eleven volumes altogether have now been issued. Several of the leading publishing houses of medical books in England are at present issuing similar series of small books. It is difficult to imagine how purchasers of books of this type can be found in the present period of enforced economy, for none of them can be looked on as necessities as they only deal with limited aspects of medical or surgical subjects which are fully dealt with in the larger books.

P. A. M.

CARDIOVASCULAR PAIN AS A BIOCHEMICAL PROBLEM.—By Gordon Lambert, B.A., M.D., B.C. (Cantab.). London: H. K. Lewis and Co., Ltd., 1933. Pp. xi plus 75, with 23 illustrations. Price, 6s.

Dr. LAMBERT's interesting and illuminating monograph dealing with the causation of angina pectoris should be regarded as a real advance in the field of cardiology, in as much as it extends a new and interesting line of research to the biochemist for finding, if possible, a biochemical solution of the problem as to the causes of cardiovascular pain. The author has collected a large number of facts in proof of his statement that the causes of cardiovascular pain cannot be wholly explained by the findings of the post-mortem examination alone, whether macroscopic or microscopic. The pathological lesions found in association with angina pectoris are found to be very variable, cases having been recorded with no recognizable lesions in the heart, aorta or the coronary arteries; on the other hand, any or all these lesions may be present without the concurrence of anginal pain.

The author seems to be of opinion that there should be a common fundamental factor which would afford a common explanation to the causes of cardiovascular pain occurring in all ages, in all degrees of severity and in all types of lesions, and even in those cases in which no demonstrable lesions could be accounted for. After carefully discussing the commonly accepted beliefs based upon hypothesis, anatomical, physiological and pathological, the author seems to think that these do not rest on secure foundations and presents the view to his readers that there must be a unity, a common link, in all forms of cardiovascular pain. According to him, this may be found in the abnormal or 'toxic' contents of the blood stream supplying the myocardium—probably the products of an abnormal metabolism. We certainly agree with the author that we have to look to the biochemist for aid in the solution of the problem of arterio-sclerosis with which the anginal pain is so closely bound up, but we hesitate to go as far as the author when he says that the 'key' to the whole problem of both cardiovascular degeneration and cardiovascular pain will be found by the biochemist who will unlock the door for both the pathologist and the physician.

J. P. B.

RADIOLOGIC MAXIMS.—By Harold Swanberg, B.Sc., M.D., F.A.C.P. Quincy, Illinois, U. S. A.: Radiological Review Publishing Co., 1932. Pp. 126. Price, \$1.50.

This is a little volume of trite sayings collected from a page devoted to this subject in the *Radiological Review* for the last six years, coupled with short statements on radiological subjects contributed by prominent physicians who are not radiologists.

It is essentially a book for the general practitioner and aims at informing him of what the radiologist can do to help him in the various departments of medicine and surgery. It is by no means a textbook of x-rays; as far as it goes it should be of considerable assistance

to the busy practitioner. There is necessarily a fair amount of repetition in the text, but this does not detract from its value as a reminder when the radiologist may be useful.

Although as a literary effort the work cannot be regarded as worthy of the highest praise it should serve a useful purpose. It is certainly worth the modest cost involved.

J. A. S.

WHITLA'S PHARMACY MATERIA MEDICA AND THERAPEUTICS.—Revised by J. A. Gunn, M.A., M.D., D.Sc., F.R.C.P. Twelfth Edition. London: Baillière, Tindall and Cox, Ltd., 1933. Pp. xii plus 645, with 16 figures. Price, 12s. 6d.

THIS well-known book needs little recommendation as it has been the daily companion of hundreds of English-speaking medical men for the last three decades.

The publication of the new British Pharmacopœia has rendered this new edition necessary and it is very welcome as its forerunner the eleventh edition appeared eleven years ago. It is with regret that we note its author Sir William Whitla was unable to edit this edition himself on account of advancing years, but the volume has not suffered at the hands of the three authorities on pharmacology to whom he has handed it over, and it may still be recommended as one of the best if not the best book for the practitioner who does his own dispensing to have always within reach.

AIDS TO PATHOLOGY.—By H. Campbell, M.D., F.R.C.P. Sixth Edition. London: Baillière, Tindall and Cox, 1933. Pp. viii plus 252. Illustrated. Price, 4s. 6d.

THE sixth edition of this useful 'cram' book on pathology has now appeared. Many parts of the book have been entirely re-written, much new matter introduced, and the book brought up to date. It is clear, concise and contains a remarkably large amount of information in an accessible form. It will prove useful to the student requiring a hurried revision of the subject.

C. L. P.

SIMPLE INSTRUCTIONS FOR DIABETIC PATIENTS.—By Dorothy C. Hare, M.D., M.R.C.P. London: H. K. Lewis and Co., Ltd., 1933. Pp. 24. Price, 1s.

THIS little book is primarily meant to be of use as a guide to patients and nurses. It contains information

of somewhat broad and general interest, such as general hygiene, exercise, dieting, and the use of insulin, and as such may prove to be of value to diabetic patients undergoing treatment, as well as to nurses having to deal with such cases.

J. P. B.

PIERSOL'S NORMAL HISTOLOGY WITH SPECIAL REFERENCE TO THE STRUCTURE OF THE HUMAN BODY.—Edited by William H. F. Addison. Fifteenth Edition. Philadelphia and London: J. B. Lippincott and Co., 1932. Pp. x plus 478, with 435 illustrations, 43 of which are in colour. [Obtainable from Messrs. Butterworth and Co. (India), Ltd., Calcutta.] Price, Rs. 18-12.

THE fifteenth edition of this very useful book has undergone thorough revision, but has preserved all the characteristic features and size of its predecessor. The sections on nerve endings, glands, and biliary passages, the epithelium of the male urethra and the cyclic changes in the endometrium have been re-written, and a number of new figures have been added. Additional references have been added to the list of selected references given at end of the book.

The information contained in the book, so far as human anatomy is concerned, is very complete and the illustrations are admirable, carefully chosen and beautifully reproduced. We have no hesitation in recommending this book to all students of medicine.

C. L. P.

INTERNATIONAL HEALTH YEAR-BOOK, 1933. Volume VI. Geneva: League of Nations.

THIS volume does not lend itself to review because by far the greater part of the book consists of statistical tables, and many of the countries contributing reports give no more than these.

The fact that the contents refer to health matters as they existed in 1929, and are only available to the public at the beginning of 1933, makes the book of small immediate value. But as a book of reference in a concise form it will be of great use to all public health authorities and should be in all libraries dealing with health matters. The statistics compiled by all the countries contributing to it have been calculated on a uniform basis, so the book is of special value, as the figures for one country are directly comparable with those of any other.

Annual Reports

ABSTRACT FROM THE CENSUS REPORT OF BENGAL, 1931. BY A. E. PORTER, M.A. (OXON.), I.C.S.

Increase of population and birth control

THE population of Bengal in this Census is 51,087,338 and equations for total populations suggest a population of between 53 and 53½ millions in 1941. The prospect or even the possibility of so considerable an increase in a population already one of the densest in the world may lead to apprehension that the population of Bengal is rapidly approaching numbers which cannot be sustained at any reasonable standard of living upon the means of subsistence which Bengal can produce for long. If population actually does increase according to some such law as that illustrated by the logistic curve the fact that considerable increases are inevitable makes the apprehension futile. Pearl himself has pointed out that this inevitable increase need not necessarily increase the misery in the world since first this result has not happened up to the present, secondly—

'the orderly evolution of human knowledge justifies us in assuming that science will keep pace in discovering

means of expanding opportunities of happy human subsistence', and thirdly the human organism is itself adaptable to an extent not yet imagined. It cannot be denied that a large part of the population of Bengal lives at a very low level of subsistence, and that any increase of population must lead to increased distress unless the potentialities of the province are developed. What is suggested here is that these potentialities are such that pessimism as to the future condition of its population if considerable increases take place is not necessarily justified. Like the rest of India Bengal is notable for its undeveloped resources and the inefficiency with which such resources as it has are exploited. The soil is probably unlikely to deteriorate further and the general opinion about areas such as Bengal, where scanty manuring necessitates small crops, is that a dead level of yield was reached long ago and is conditioned by the rate at which plant food constituents are made available by weathering. The cultivator in Bengal practically never enriches the soil with any manure and the use of manures together with an improvement in the implements of agriculture which would then be rendered possible would probably increase enormously

the output of the soil. It has been estimated that improved methods would result in a reasonable expectation of increased food output of 30 per cent throughout the whole of India. There is no doubt that any additional labour required under a more intensive form of cultivation could easily be obtained since the agriculturist in Bengal on the whole probably works less than agriculturists in almost any other part of the world, also of the total area cultivable only 67 per cent is now actually under cultivation. If the total cultivable area were brought under cultivation and if improved methods of cultivation yielding an increase of 30 per cent over the present yield were adopted it is clear from a simple rule of three calculation that Bengal could support at its present standard of living a population very nearly twice as large as that recorded in 1931. Fresh areas in course of time will be brought under cultivation as lands on the Bay of Bengal accrete and reach a stage suitable for cultivation. Even at present it is clear that by far the majority of the food-stuffs consumed in Bengal are locally produced. During 1930-1931, taking only grains, pulses and flour, salt, sugar and spices, provisions and oilman's stores Bengal imported goods of the value of Rs. 821 lakhs and exported goods of the value of Rs. 281 lakhs. But the balance of trade during the same year amounted to Rs. 34,52.41 lakhs or more than three times the aggregate export and import trade. The sea-borne trade of Calcutta is not confined to goods originating in or meant exclusively for Bengal, but in the year 1930-1931 jute, tea and hides contributed 77½ per cent of the total and Bengal contributed all the jute, nearly all the hides and a very considerable part of the tea. It is consequently clear that the favourable balance of trade to a very small extent only was dissipated outside Bengal and that the balance itself provides sufficiently for an enormously increased importation of food-stuffs were it necessary to import them at any time. Not only agriculture but also industry is at present in Bengal practically in its infancy. Reviewing production in India a Bengali writer in 1924 came to the conclusion that the— 'outstanding feature of the productive system of India is its inefficiency which is shown by the great wastage of resources on the one hand and the lower productivity of the industries on the other It is insufficient production to which is due India's poverty, both absolute and relative The lack of capital is partly responsible for the present low productivity but could not be regarded as the fundamental cause of insufficient production in India Insufficient production is the result of inefficient labour, i.e., lack of capacity on the part of the people to mobilize the physical, intellectual and moral forces of the country and to organize land and capital effectively for national production'. Improvement in methods of production both agricultural and industrial should, therefore, very easily make possible the subsistence of such an increased population as is suggested by the figures already discussed and the considerations deduced in this paragraph also make it possible to hope that such an increase of population may be attended with a very considerable increase in the material condition of the people and in the standard of living. It is clear at least that it is not yet time to indulge in gloomy forebodings on the grounds that Bengal is over-populated, provided full use is made of the available resources of the country by improved methods.

A final problem suggested by the growth of population in Bengal concerns the enormous wastage of life with which that growth is achieved. It is clear that what is of importance in population growth is the rate of increment. A high rate of increment can be achieved by a relatively low birth rate if the death rate is also low, whilst on the contrary a comparatively low rate of increase results from even a high birth rate if the death rate also is high. Actually both the birth rate and the death rate in Bengal are very high and there is consequently an appalling wastage of reproductive energy in

maintaining the present increase of population. If the logistic theory of population growth is correct a retarded rate of increase is inevitable at the upper stages of the cycle of growth until finally a population is reached which to all intents and purposes is stationary. France in Europe where there is a notoriously low birth rate probably illustrates this position best but an exhaustive enquiry into the Arab population of Algiers suggested to Pearl that the retardation of the rate of increase is in general effected at the upper stages of the population growth by decrease both in the birth rate and in the death rate. The Arab population of Algiers showed both a decrease in the birth rate which could not be ascribed to any voluntary measures and a decrease in the death rate which equally could not be ascribed to improvement in public health measures since the traditional customs of the Arabs offer the utmost possible resistance to any changes in their habits which would improve sanitary conditions. Attempts to effect a retardation of the rate of increase by voluntary limitation of the birth rate are almost certainly doomed to failure particularly in Bengal. They are repugnant to common sentiment in this country, the methods adopted are so expensive as to be beyond the reach of the great majority of the inhabitants and it is probably true to say that there are as yet none which can be relied upon as being absolutely certain and satisfactory. Figures for the different strata of society show that there is no evidence that contraceptive measures are used by the upper classes or those engaged in professions and the liberal arts; and it is certain that they are not practised at all in the lower strata of society. What appears to happen, if the analogy of Western Europe may be accepted, is that a decrease in the birth rate is inevitably followed at some period by a corresponding decrease in the death rate. It is clear also that fertility in western countries decreases with the increase of wealth and intellectual interests. It is therefore possible to expect that a reduction of the birth rate by the adoption of improved measures of public health accompanied by an improvement in the standard of living, an increase in the spread of education and perhaps principally by a further emancipation of women and their introduction to spheres of usefulness and activity from which they are now in Bengal generally debarred by social custom and by the institution of purdah will in due course result in a decrease in the birth rate corresponding with the decrease in the death rate which it is the object of public health measures to bring about.

ABSTRACT OF THE REPORT OF THE GOVERNMENT OF MADRAS, LOCAL SELF-GOVERNMENT DEPARTMENT (PUBLIC HEALTH). (CIVIL HOSPITALS AND DISPENSARIES—TRIENNIAL REPORT—1929-31)

THE following brief abstracts from this report will show that Madras, always one of the most progressive sections of India regarding medical education and the care of its sick, is still advancing although severely hampered by the universal economic difficulties of the present time.

One of the chief features of recent medical development has been the opening of an increasing number of rural dispensaries, to the medical officer in charge of which Government gives a subsidy in proportion to his qualifications and a further subsidy for a midwife. Sometimes these subsidies are added to by the taluk boards who control these dispensaries. At the close of the last triennium there were 326 of these subsidized dispensaries; at the end of the present triennium there were 506 in operation.

Medical education has improved considerably in the medical colleges, while the bigger medical schools have benefited by the closure of the less important schools and the concentration of teaching talent in the larger centres. The medical schools, however, require a considerable further improvement before we can be satisfied

that we are giving the best possible teaching with the means at our disposal.

Several minor improvements in the licentiate course have been carried out and others are still under the consideration of Government. The more important of the latter are those to raise the examination standard and to extend the L.M.P. course to five years.

Medical inspection of schools.—The Government requested the Surgeon-General to formulate an experimental scheme for introduction in two districts.

On a rough calculation, the routine inspection of school children in the two districts suggested was estimated to cost Rs. 56,000 a year. The Government observed that the extension of a scheme of this kind to the whole Presidency would involve an annual expenditure of many lakhs. While the Government do not underrate the importance of medical inspection in schools they were constrained to observe that the present scheme is far beyond anything that the provincial finances can afford. The Director of Public Instruction was therefore requested to work out in consultation with the Surgeon-General a less expensive scheme which it would be possible to introduce in selected areas in the first instance and which would be capable of expansion as funds permit.

The total number of medical institutions of all classes working in the Presidency at the beginning of the triennium under report, i.e., on 1st January, 1929, was 1,089 and 1,245 at the end of 1931, i.e., 1,005 in rural areas and 240 in urban areas. There were thus 156 institutions more at the end than at the beginning of the triennium. The increase is due to the opening of additional subsidized rural dispensaries.

In 1929 Doctor Santra of the British Empire Leprosy Relief Association, Indian Council, New Delhi, carried out leprosy survey work in the districts of South Arcot and East Godavari in this Presidency and opened leprosy clinics in those districts. The survey had the effect of stimulating the interest of district boards and six of them have appointed leprosy officers in their respective districts.

The actual number of lepers in the Madras Presidency has been estimated in various ways and with a considerable difference in the totals arrived at. Thus

1921 Census	16,595
1931 Census	33,069
Health Department investigation in 1930	48,000
Rough expert estimate	100,000

Doubtless one reason for the apparent increase in the number of lepers is that owing to propaganda and evidence from the leprosy clinics that the disease is not hopeless, but can usually be arrested when the patients come early, the patients are now coming forward more readily instead of endeavouring to conceal their disease.

Midwifery.—The total number of labour cases conducted in all classes of medical institutions during 1931 was 140,403 normal and 15,003 abnormal. This branch of activity has more than doubled in the last six years.

Radium.—Radium has been used increasingly by the surgeons attached to the large hospitals in Madras and Vizagapatam, and is found to be of the greatest value. Government now possesses over 600 milligrammes of radium of an approximate value of Rs. 1½ lakhs.

Honorary medical officers.—The scheme of appointing honorary medical officers to all district headquarters and government hospitals in the mofussil was introduced in 1929 and several officers were appointed. The scheme has made considerable progress as many private medical practitioners with special attainments in the branches of medicine and surgery were appointed as honorary medical officers in the city state hospitals as well as in the mofussil.

At the beginning of 1929 there were only 9 honorary medical officers working in government hospitals and at the end of the triennium there were 90 and the number is still increasing.

It has been calculated that without our existing staff we should, to deal with the same amount of work, have

to employ more medical staff at a cost of Rs. 1,85,000 per annum and the honorary staff may therefore be considered to be saving Government this amount annually.

During the last year of the preceding triennium was formed the Madras Nurses and Midwives Council to establish a register of trained nurses and midwives and to supervise the standards of education in these occupations. The council has now on its registers 618 nurses, 1,353 midwives and 6 dhais. The Nurses and Midwives Council has also arranged reciprocity of recognition as regards qualifications with the General Nursing Council for England and Wales and the Joint Nursing and Midwives Council of Northern Ireland. The registration performed by this council is believed to be the only registration of nurses and midwives so far in India under an Act of the Legislature.

ABSTRACT OF THE ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF BIHAR AND ORISSA FOR THE YEAR 1931

The use of bacteriophage

THE districts of Muzaffarpur and Purnea were selected for the experiment for the following reasons:—

(1) Because they are regarded as the worst cholera districts in their respective divisions of Tirhut and Bhagalpur.

(2) Each of these districts has a well-organized health staff through whom it was proposed to distribute bacteriophage, both for preventive and curative purposes, and to obtain fairly accurate data regarding the case incidence and mortality from cholera.

(3) The two districts are relatively well provided with roads, except in one section of Purnea, which render most villages in the district fairly easily accessible.

During the whole course of the experiments, no inoculations were carried out in either district, and no disinfectants were used. Essential-oil mixtures for the treatment of cases were not permitted, and as far as possible bacteriophage alone was used for the treatment of cases.

The experiment brought out many interesting facts some of which are:—

(1) It was definitely established that the duration of an epidemic was considerably shortened when bacteriophage was used. Thus the average duration of a cholera epidemic in a thana area where the usual methods of dealing with an outbreak are employed has been estimated as 83 days. In these two districts where bacteriophage was used the epidemic subsided completely in 14 days. Similarly, in villages the average duration of an epidemic has been estimated as 23 where the usual methods are employed, whereas it only lasted 3 days in villages in these two districts where bacteriophage was used.

(2) Although cholera was not as severe as usual in 1931, the mortality from cholera in these two districts was not only the lowest amongst the districts in their respective divisions, but the lowest in the whole of North Bihar.

(3) Financially there was a considerable saving of money to the two district boards, as no disinfectants, and no other remedies for the treatment of cholera were purchased. Government was also saved the cost of cholera vaccine which would otherwise have had to be supplied to the districts.

(4) Bacteriophage is tasteless, colourless, and odourless, and not only was the treatment of wells with it not objected to, but the villagers actually asked for it when they had once had it in their wells—a very different story to what happens when an attempt is made to chlorinate wells.

Unfortunately no very spectacular result was obtained during the year under report with bacteriophage. It was a mild cholera year and although other districts in North Bihar reported more attacks and deaths than

these two districts, their figures were also lower than usual. A conclusive verdict in favour of its adoption throughout the province has been deferred, and the experiment is being continued in the same two districts in 1932.

The sale of quinine treatments at the various post offices in the province has been in force for many years. The sale during 1931 amounted to a total of 536.4 pounds of quinine sulphate as compared with 501.2 pounds in the previous year.

At Puri the year under review was of special interest as the Nabakalebar ceremony had to be performed during the Rath Jatra. The ceremony, which consists in the complete renovation of the wooden figures representing the three deities in the temple of Jagannath, is performed at long intervals, generally about 18 years. The last ceremony of the kind took place in 1912. Pilgrims to Puri in these years acquire special merit, and the attendance in these years is usually more than double that of an ordinary year. In 1912 the total number of pilgrims estimated to have visited Puri was about 250,000 but no details of these figures are given. It is not easy to arrive at the figures for 1931 but 161,550 is considered to be a fairly accurate estimate.

To prevent a recurrence of what happened at Puri after this ceremony in 1912, when no less than 1,053 deaths were recorded in the town itself, and the serious epidemic which followed in the Puri and neighbouring districts, special measures were taken by the public health department, the municipality, the district board and the Bengal Nagpur Railway authorities.

Government sanctioned the employment of a special temporary staff of doctors for the supervision of the sanitation in the town, for inoculation in the town and at the railway station at Puri, and for inoculation duty at Cuttack and Balasore. The municipality engaged an extra staff of sweepers for the sanitation of the town. The district board established inoculation centres along the roads traversed by pilgrims from the district, and the railway authorities arranged for the inspection of pilgrims travelling by rail at the important junction stations, established eight disinfecting stations between Kharagpur and Puri, and provided sheds for camps and camp hospitals at certain stations where hospital accommodation did not exist.

The engineering branch of the public health department installed six engine-driven pumps with connected tanks and taps at six of the more important wells, and ten hand pumps at other wells, and the municipality arranged for hand pumps at sixteen other wells and sank 31 small tube wells.

Except in wards 4 and 5 of the town, where bacteriophage was used, the whole of the remaining wells were chlorinated throughout the *mela* period.

Inoculations with cholera vaccine were commenced in April in the town of Puri amongst the permanent residents, and as the immunity conferred by these early inoculations persisted through the *mela* period these figures are included in the totals given below. The figures however for the district are only those done amongst definite pilgrims to Puri for the Rath Jatra—

Total number of inoculations done in the town	34,226
Total number of inoculations done in the district	43,249
TOTAL	77,475

In addition to these figures a total of 6,643 inoculations were carried out in the Cuttack and Balasore districts amongst pilgrims proceeding to Puri, so that the total number of inoculations carried out in the province in connection with this festival was 84,120. This does not include the number inoculated by the public health department of Bengal.

An attempt was first made to protect pilgrims attending Puri for the Snan Jatra and Rath Jatra in

1927 and the following figures are of interest as they illustrate the steady progress that has been made with this important preventive measure. These figures are only for the town itself, and for a short period immediately preceding the Snan Jatra and following the Rath Jatra.

Year	Number of inoculations
1927	7,937
1928	16,869
1929	32,155
1930	42,047
1931	34,226

The figure for the town in 1931 would have been still higher, if the district board arrangements for the inoculation of pilgrims travelling by road had not been so complete.

There was no little anxiety in the public health department during the course of the *mela*. Cholera was prevalent in all the districts of Orissa, more especially in the district of Puri itself, and cases of cholera were actually occurring in Puri town at the time. But the elaborate precautions taken, and the thorough arrangements made were entirely successful as the following figures show. There were only 73 cases of cholera in the town during the *mela*, i.e., up to 31st July, and only 9 deaths as against 1,053 deaths in 1912.

ABSTRACT OF THE ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF ASSAM FOR THE YEAR 1931

A TOTAL of 5,523 deaths from cholera were reported from Assam in 1931, as compared with 6,332 in 1930. The death rate per mille of population for the year 1931 was 0.70 as compared with 0.92 in 1930 and 1.53 the decennial average. The decrease in the incidence of cholera and smallpox in 1931 as compared with that in 1930 and the decennial average is partly due to the limitation of movements of individuals resulting from financial stringency.

During the year a provincial malaria committee was constituted with the Inspector-General of Civil Hospitals as president, the principal, Ross Institute, the research officer, Assam Medical Research Society, Director of Public Health, secretary to the Government of Assam in the transferred departments and the secretary, Assam Medical Research Society, as secretary to consider and advise Government on all malaria schemes. The object in forming the committee is to obtain co-ordination between various authorities interested in the malaria problem in the province. Malaria is endemic in Assam and it is hoped that the problem will be successfully tackled by the co-operation of the parties concerned.

The number of deaths from kala-azar rose slightly by 64 from 953 in 1930, to 1,017 in 1931. The Kamrup, Darrang and Goalpara districts contributed to the increase. The increase which is insignificant does not require any explanation. The number of patients treated fell from 16,430 in 1930 to 9,759 in 1931. The method of diagnosis of kala-azar adopted was as usual by the formolgel test and by clinical signs and symptoms. Treatment throughout the province is by means of intravenous injections with urea-stibamine. This treatment is wholesale and free. A limited experiment with neostibosan is being undertaken in the Kamrup district. Special attention is being paid to intensive and detailed surveys in order to detect fresh cases. Villages within a certain radius of dispensaries in kala-azar-infected districts are surveyed by the medical officers in charge. Sub-assistant surgeons are specially deputed to survey other areas where a recrudescence of the disease is suspected. In Cachar all suspected villages in the Hailakandi subdivision were surveyed during the year and all cases detected were brought under treatment. On account of a marked decline in the number of cases, the special kala-azar indoor wards at

Habiganj, Sunamganj and Sylhet sadar hospitals were closed during the year. Three outdoor dispensaries in this district were closed as they were no longer necessary and one was opened. Intensive surveys were undertaken in different parts of the Goalpara district, resulting in the necessity for opening three new out-centres. Intensive surveys were carried out in the Kamrup district and this resulted in the necessity for opening two new dispensaries and four out-centres. Four kala-azar dispensaries had to be closed. The indoor kala-azar wards attached to the Gauhati and Barpeta hospitals were transferred to the Medical Department as the necessity for their retention ceased to exist. Two kala-azar dispensaries in the Nowgong district and three in Sibsagar district were closed owing to the reduction in the number of kala-azar cases in those districts. The Garo Hills district was surveyed for kala-azar cases by four hill-men sub-assistant surgeons as in the previous year. During the year the number of beds in the Tura kala-azar hospital was reduced from 200 to 100 owing to the fall in the number of patients.

During 1931, 5,895 deaths from respiratory diseases were returned, as compared with 5,859 in 1930.

A campaign against yaws was started in January 1931 in the Digarukhetri area by the civil surgeon of the Kamrup district. The disease was first detected in 1929 in this area by Dr. Nepal Chandra De of the kala-azar department. The ravages of the disease were responsible for much suffering and mutilation amongst the Mikirs and Lalungs who inhabit this area. The benefits of treatment were soon realized and the people came forward in increasingly large numbers. A total of 735 cases were treated at Digaru, Kapalkata, Khetri and Verakuehi. To the west of these dispensaries, cases were found amongst Rabhas, Kacharis and Khasis inhabiting the submontane region around Boko. At the local board dispensary at Boko, 66 cases were treated and a few also at the Hahim kala-azar dispensary. A large number of drugs were given a clinical trial, first supplies in most instances being obtained free through the courtesy of the manufacturers. An endeavour has been made to standardize a satisfactory course of treatment. The question is one of obvious importance in view of the widespread distribution of this disease throughout Assam. The results are not yet complete. The civil surgeon, Kamrup, believes that well-established yaws is as resistant to cure as syphilis and has to be treated with corresponding thoroughness.

ABSTRACT OF THE ADMINISTRATION REPORT OF THE DIRECTOR OF MEDICAL AND SANITARY SERVICES, CEYLON, FOR 1931

THE hookworm campaign begun fifteen years ago is still being vigorously prosecuted but 79 per cent of the total population of the island is still infected.

Reorganization of the units engaged in this work has resulted in a saving of over Rs. 80,000 but in spite of this the number of treatments given was greater than during the previous two years and the third highest that has ever been given in a single year.

The actual number treated was 1,406,406 and one death is recorded. This was in a child aged ten years*

* (Note.—As the routine dose for children of this age is 9 minims, according to the 1930 report, it seems possible that the child referred to above may have presented certain contra-indications and have been given a reduced dose accordingly. Therefore the fault in this case appears to have been rather in giving the dose to an unsuitable case than that the drug exhibited a surprising and unusual effect in a healthy person. The latter is the usual excuse advanced for deaths from anthelmintic drugs but, in our opinion, if the real facts could be elicited in deaths of this kind, it would be found very frequently that the victims were suffering from some condition that a brief clinical examination would have revealed and the existence of which should have exempted the particular individual from treatment on that occasion.—EDITOR, I. M. G.)

who received a dose of 5 minims of oil of chenopodium and died 76 hours afterwards. Up to the age of ten years oil of chenopodium alone is given and all persons over the age of ten receive a mixture of carbon tetrachloride and oil of chenopodium graduated according to age. The maximum dose employed in adults is 30 minims of carbon tetrachloride and 10 minims of oil of chenopodium. This is somewhat less of both drugs than is usually employed but as it appears to be fairly efficient and safe there is nothing to criticize in this.

A preliminary investigation of hexylresorcinol is reported; 52 hookworm cases with 21 per cent cures, and 45 ascaris cases with 49 per cent cures are recorded.

As the test of cure appears to have been a negative result using Stoll's dilution technique the cure rate is probably much higher than if Lane's centrifuge had been employed. The drug is said to have been supplied by the Rockefeller Foundation and so one of the great objections to it, viz, the price, is not appreciated by the Ceylon authorities. If the drug had been purchased and the recommended dose of 1 gramme given to each of the patients treated the cost of this small investigation for the drug alone would have been between 60 and 70 rupees.

TRIENNIAL REPORT ON THE WORKING OF THE HOSPITALS AND DISPENSARIES IN BIHAR AND ORISSA, FOR THE YEARS 1929, 1930 AND 1931

THE following abstracts from this report are applicable to other provinces besides the one in which they have been written, for a similar state of affairs exists in many parts of India.

Hospitals and hospital maintenance.—The principle followed has been that medical relief should be not only a charge on public funds but that it should be also managed by public officials, be they State or otherwise. This principle was inevitable from the inception of medical relief in this country and the people have never been educated to expect that this method is other than the only one that is applicable or necessary for the province.

But there is every reason to suppose that when local bodies instituted a subscription list in their hospitals and dispensaries, that after the initial outlay of expenditure in constructing and equipping such institutions, it was expected that the people in the locality should help to support these institutions, not only for their own benefit but for the benefit of the districts and country at large.

The entirely self-supporting dispensary maintained by public charity similar to the cottage hospital in England was perhaps the object of instituting subscription lists and managing committees, but if so, the dream has not materialized. The only institutions that are really charitable institutions in the province are class V dispensaries maintained entirely at the expense of some public-spirited gentlemen who have a commendable consciousness of civic responsibility.

With the twofold intention of preventing abuse of hospitals and obtaining monetary local assistance, the institution of a small fee for well-to-do patients was recommended for the consideration of the district boards in 1927. The response to this appeal throughout the province up to very recently was of a negative nature.

Local support therefore to any dispensary or hospital as regards maintenance can be ruled out as non-existent and the onus of upkeep is dependent on public funds. If we admit as we must admit for this province that medical relief is a charge on public funds, we must recognize that the people themselves are apathetic in contributing to any institution where it is believed and acted upon, that any needs of the institution will be met from public funds. This apathy is comprehensible and until the impression is created that the time has arrived for the charitable instincts of the people to be guided into this deserving channel, further progress will be difficult. That the people themselves are not

uncharitable is obvious from everyday observation, but that they should contribute to an institution which is being maintained by public funds is another matter, and the imposition of a small fee which has been advocated and commenced in some institutions in this province may be viewed from the angle of educating the people to the needs of the sick poor, as much as that it should be considered as a competent source to diminishing the burden of maintenance charges.

There is another important point to be considered in this connection, *viz.*, the ever-growing number of medical men turned out from the schools and colleges who have to earn a livelihood; in those localities where free treatment is obtained from the hospitals the imposition of a fee on the well-to-do patients will assist these struggling practitioners.

Medical personnel.—At present the medical relief of the remoter parts of the district falls upon the hospitals and dispensaries in charge of doctors of the licentiate class. These doctors have qualified from the medical schools in this province generally and to a smaller extent from the Bengal Province, but the latter are gradually being replaced by the licentiates of the schools of this province.

One must record however that the standard of efficiency of the doctor in charge of local fund dispensaries is below what it should be. I am taking the cadre as an average and fully recognize that there are brilliant exceptions but my experience of the average licentiate in the employment of district boards is that they are not good examples as disciples or exhibitors of the advantages of a scientific training in medicine.

The main causes of this state of affairs are twofold, one dependent on the standard of training received at the medical schools which will be discussed later, and the other on the inherent defects in the doctor himself. The average L.M.P. in district board employ is cast on his own resources in outlying and isolated dispensaries and neither opens a medical book nor has any ambition to do so. This may appear to be strong indictment against the professional capacity of the licentiates, but even if it is overstated it is important in the present times owing to the tendency of the district boards to build dispensaries in which medical officers are appointed who are disciples of one of the indigenous medical systems.

It was stated in the last triennial report that 'western medicine at its best has nothing to fear from a comparison with the indigenous systems of medicine', but the qualification 'at its best' tends to confuse the issue, and in general medical relief in the province we are not concerned so much with the exceptions but with the average; and if our policy is that medical relief should be in the hands of the people best qualified to give that relief we should periodically take stock of the standards of qualification.

The standard of efficiency of the medical officer is intimately related to the policy now advocated of charging fees at hospitals and dispensaries.

Nursing.—Most of the hospitals are without any nursing arrangements. Their limited funds cannot afford to pay for Anglo-Indian nurses while Indian nurses are not easily available owing to the absence of training centres and of a suitable syllabus for training.

Medical education.—The difficulty of newly-qualified practitioners in finding employment is already becoming acute; the number of applications received for vacancies in Government service is an indication of the trend of events and it is a matter for consideration as to the extent the administration is concerned with the overcrowding of the profession.

This statement of overcrowding requires examination. If counting heads was the only consideration then the proportion of medical men to population is not excessive and no overcrowding is apparent.

But whereas in a country like England the proportion of medical men to population may be placed in round figures at one in 1,000 yet such a comparison is useless for this country. The mass of the people live in

villages and the average wealth of the occupants is not such as to guarantee a living wage to any qualified medical officer settling down in such a community; the result is that the medical practitioners are compelled to flock to the larger towns and it is in these large towns that the evidence of overcrowding is so apparent.

This overcrowding is without doubt leading to a lower ethical standard amongst medical practitioners and although this may be considered as inevitable, the administration will be forced eventually to face this question and as it is a difficult one, not to dodge it, but to overcome it. The position as I see it is as follows:—

(1) Young men are being educated in larger numbers every year and it is inevitable therefore that a large proportion of these masses will join the medical profession as one of the outlets for an educated man.

(2) The limitation of entries into the medical schools or colleges of the province will not solve the problem so long as the medical men from other provinces are allowed to settle down here and practise with only the medical registration fee to pay.

(3) The protection of the qualified man from quacks, charlatans and other species of that ilk that infest both large towns and the country villages is a matter which however should receive careful consideration and is one which not only affects the qualified medical practitioners but the general public also. Just as the agitation has commenced to protect the public in this country from quack medicines, so it is time for agitation to commence on the *bona fides* of not only the ammunition but the gun that fires the ammunition, and the latter is of greater importance.

(4) The steady increase in the numbers of lady doctors which will inevitably take place further complicates this question and is one that will affect this country with its customs and prejudices much more than other countries.

The importance of raising the standard of the sub-assistant surgeon is intimately related to what has been said with regard to overcrowding of the medical profession.

If graduates are finding a difficulty in obtaining employment after qualification, it is not difficult to visualize that in the future the out-patient dispensary may receive some of the surplus stock of these graduates at the expense of the licentiates. The course of events will follow the laws of supply and demand and when the supply exceeds the demand, the price of the commodity will be lowered, and the district boards and local bodies will naturally prefer to obtain the services of a cheap but efficient assistant surgeon rather than a cheap but mediocre licentiate, and this obviously will be to the benefit of all concerned.

What then is to be the position of the licentiate? Is that body of very useful citizens who were the pioneers of scientific medicine in this country to be crowded out by a better qualified man, or is that cadre to be raised from its present standard to a position where it can still compete and hold its own with the average practitioner? We must take it for granted that the first recommendation to be made to raise the standard of the licentiate will be to prolong the curriculum by another year to five years, which will bring it into line with the curriculum required by graduates but will *ipso facto* increase the cost of training. The fact that at present the poorer classes can obtain a licentiate degree in allopathic medicine is one that is all important, and whereas want of funds may debar many deserving students from qualifying as graduates, this is perhaps subsidiary to the lack of the higher standard of preliminary education which is necessary for a graduate, and which higher standard the parents have not been able to afford. It would appear then that if riches are not to impede the aspirations of the poor student in obtaining a qualification in allopathic medicine the obligation to maintain the licentiate is a real one; but as stated above there is on the other hand the obligation on the administration that if the

licentiate is to be retained he should be of such a standard of efficiency that he should be able to maintain the good name and repute of scientific medicine.

Moreover if it is admitted that qualification in the medical profession is not the end but the means to the end, and after qualification as the licentiate has equal opportunities with the graduate to make good, the policy of retaining the licentiate is justified.

ABSTRACTED FROM THE ANNUAL REPORT OF THE DIRECTOR, INSTITUTE FOR MEDICAL RESEARCH, FEDERATED MALAY STATES, FOR THE YEAR 1931. KUALA LUMPUR: PRINTED AT THE FEDERATED MALAY STATES' GOVERNMENT PRINTING OFFICE. 1932

The opening sentence of this report is typical of most publications of this nature that we are receiving just now, it reads as follows:—'The shrinkage in public funds consequent upon the present universal economic crisis has not been without influence on the activities of the Institute.'

But when we turn to the detailed record of the work done we cannot see where the Institute's activities could have been curtailed for if we take malaria alone it is difficult to imagine how a fuller year of work could have been carried out by a single institution. The work on malaria is so many-sided and the amount of information supplied is so great that on account of limitations of space only a small part of it can be abstracted; we have therefore confined our abstract to report on drug prophylaxis and therapeutics.

MALARIA Prophylaxis

An experiment on the prophylactic value of plasmoquine simplex when exhibited twice weekly in an adult dose of 0.04 grammes was completed. The venue of

improvement in the general physical condition of the labourers was very satisfactory, an observation which was confirmed by the sick rates. The total sick rate fell by 51 per cent on the experimental estate, by 11 per cent on one of the control estates, but rose by 21 per cent on the second control estate.

Quino-plasmoquine

In a malarious village near Kuala Lumpur there had been a number of cases of clinical malaria among the police force. Permanent anti-malarial work was out of the question, and it was suggested that quino-plasmoquine might be employed for its prophylactic effect. The police, including dependants, totalled 63, and, at an examination before the commencement of treatment, the spleen rate was found to be 10 per cent and the parasite rate 5 per cent. The dosage adopted was 2 tablets daily, i.e., 0.02 grammes of plasmoquine plus 0.6 grammes (9 grs.) of quinine. For the first week this preparation was taken daily, but on successive weeks it was taken on Mondays, Tuesdays and Wednesdays only.

Since the application, in October, of this form of prophylaxis there has been one case of sub-tertian malaria in a policeman who was parasite free at the time of the preliminary survey. There is doubt, however, if he had taken the drug regularly. An investigation of the urines, passed by the police, indicated that a number of the men were probably avoiding treatment.

THERAPEUTICS

During the year several drugs have been submitted to this Institute for testing in regard to efficacy in the treatment of malaria. Including control cases, 169 individuals have been specially treated and observation has been continued after the termination of treatment for periods varying from a few days to several months. The number of cases, together with the drug and daily dosage, are summarized in the following table:

DRUGS AND DAILY DOSAGE

Type of malaria	Quinine bihydrochloride gr. xx	Quinine bihydrochloride gr. xxx	Quinine bihydrochloride gr. vi	Quinine-stovarsol gr. xii	Malarcan 12 tablets	Atebrin ('Erion') 0.2 to 0.4 gm.
B.T. ..	10	14	6	13	1	13
S.T. ..	8	11	1	10	8	18
Q. ..	9	19	6	12	1	9
TOTALS ..	27	44	13	35	10	40

the experiment was a malarious rubber estate with a population of about 330. Two adjacent estates with populations of 405 and 362 served as controls, and quarterly surveys for parasite and spleen rates, hæmoglobin percentage, and anopheline breeding-places were undertaken on the three estates.

As regards sub-tertian malaria, the results, judged from the parasite rates, were somewhat inconclusive, but, towards the end of the experiment, no *P. falciparum* gametocyte carriers were found on the experimental estate. The method of prophylaxis was found to be less satisfactory for benign tertian malaria, and it was concluded that plasmoquine has, perhaps, a less definite gametocidal action on *P. vivax* than on *P. falciparum*.

On the other hand, the effect of the measure on the incidence of clinical malaria was definite. In the twelve months preceding the experiment, the sub-tertian and benign tertian cases totalled 30.4 and 52.5 per cent of the population on the experimental estate, i.e., a total of 82.9 per cent. Throughout the experimental period the incidence was 7.0 and 8.7 per cent for sub-tertian and benign tertian, i.e., a total incidence of 15.7 per cent only. The fall in the splenic index and the rise in the average hæmoglobin percentage were small, but the

Atebrin ('Erion')

A new preparation, which tentatively was given the name of 'erion' and is now to be known as 'atebrin', has recently been produced by the makers of plasmoquine.

The supply was received in the form of tablets. The drug is somewhat bitter to the taste and is fairly soluble in water to which it imparts a bright yellow colour. Unlike plasmoquine, but like quinine, it shows fluorescence under ultra-violet radiation.

The investigation of its properties is still proceeding.

Up to the present, 40 cases have now been treated with this new synthetic drug. It compares favourably with quinine on all counts except in the rate of destruction of the trophozoites of *P. falciparum*. The drug is not unpleasant to take and no marked toxic symptoms have yet been observed, though a temporary yellow discoloration of the skin and sclerotics sometimes occurs. The dosage employed was about one-seventh of that for quinine. According to the tables accompanying this portion of the report no relapses occurred in any of the three types of malaria treated with atebrin whereas there were 5/13, 3/15, 5/19 relapses in

control cases of benign tertian, malignant tertian and quartan respectively, which were treated with quinine.

Quinine-stovarsol

Work on this drug has been continued, and comparisons made with cases of sub-tertian, benign tertian, and quartan malaria, treated with quinine-stovarsol, 0.75 grammes (12 grains); quinine bihydrochloride, equivalent in dosage to that contained in the quinine-stovarsol, i.e., 0.37 grammes (6 grains); 20 grains of quinine bihydrochloride and 30 grains of quinine bihydrochloride daily.

The results of these treatments have been compared with reference to the rate of disappearance of parasites; the occurrence of relapses; the relief of symptoms; gametocidal properties; the reduction in the size of the spleen, and the increase in haemoglobin percentage and in the number of erythrocytes.

The general conclusions may be briefly stated as follows: The stovarsol contained in quinine-stovarsol has a definite parasitocidal effect on *P. vivax*. Twelve grains of quinine-stovarsol daily is as effective in benign tertian cases as 20 or 30 grains of quinine, but the former drug has the disadvantage of being less efficacious in quartan and sub-tertian malaria and is therefore of little use in apparent, or concealed, cases of mixed infections. Further hyperpyrexia and exacerbation of symptoms may occur during the first twenty-four hours of treatment in all three types of malaria infection. It is not superior to quinine in regard to the prevention of relapses, and is without action on sub-tertian gametocytes. One crescent carrier, after continuous treatment with quinine-stovarsol for 25 days, infected anopheline mosquitoes, and hence the drug can have little effect on the viability of the sub-tertian gametocyte. With these disadvantages there appears to be little place for quinine-stovarsol in tropical practice, particularly as the preparation is about five times more costly than quinine.

Malarcan

This preparation is said to have the formula methyl-acridine-methyl-cupreine-dehydrocholate; that is, a compound of a stereo-isomeric base of methyl-cupreine (quinine contains methyl-cupreine as part of its structural formula while the stereo-isomer of quinine is quinidine) combined with methyl-acridinium-chloride and dehydrocholic acid. Malarcan, in high dilutions, like quinine, shows fluorescence under ultra-violet light.

A supply was obtained sufficient for the treatment of ten cases, including one quartan, one benign tertian, and eight sub-tertian infections. Twelve tablets of malarcan were found to alleviate symptoms and to destroy parasites as effectively as quinine in a dosage of 30 grains. Cases were treated for from 7 to 14 days and subsequently kept under observation for periods ranging from one to six weeks. No relapses were observed. The effect on the gametocytes of *P. falciparum* was, however, negligible and, in view of the fact that the cost of malarcan is approximately six times that of quinine, it is unlikely that its use will become general.

Control cases treated with quinine

Quinine was exhibited to control cases in a daily dosage of 30 grains of the bihydrochloride, and certain points of interest have been noted from a close study of them. Quartan trophozoites and schizonts may persist in the peripheral blood for two days after the completion of seven days treatment. In similarly treated cases, quartan gametocytes were demonstrated in the peripheral blood five days after the cessation of the course.

Careful measurement has shown that in some cases the spleen becomes larger during the first two days of treatment, but subsequently, with the disappearance of parasites, its size diminishes. This initial enlargement may be due to the increased activity in destroying quinized parasites and damaged red cells.

Despite preliminary purgation, the absorption of quinine during the first three or four days of treatment appears sometimes to be irregular, if gauged by the quantity excreted in the urine. The disappearance of parasites from the peripheral blood is delayed in such cases.

When patients first came under observation, the parasites found in the peripheral blood may have been sub-tertian or quartan. But, after a relapse, benign tertian parasites only have not infrequently been found. Similar observations have been made by Fletcher in this country and by others elsewhere. The finding indicates that an unexpectedly large number of malarial infections in Malaya are, in fact, mixed, but, during the acute stage, one type or another dominates the picture and is the only one identified. The other type of parasite probably sporulates quietly in the blood stream and occurs in such small numbers that it is not evident in either thin or thick films.

Cinchona febrifuge

The chief objections to cinchona febrifuge are its varying composition and the trouble in dispensing. Solutions must be rendered more acid to ensure solution than is the case with quinine sulphate, and unless carefully filtered, are often slimy and unpleasant. Further, cinchona febrifuge contains a large proportion of amorphous cinchona alkaloids (Indian febrifuge, 45 per cent; Java febrifuge 37 per cent) and these amorphous alkaloids are relatively toxic and liable to produce vomiting, dizziness, etc. It not infrequently happens that the Tamil estate labourer refuses to swallow this preparation.

Although this is all we have abstracted, workers on any branch of malaria will find something about their special subject which is worth perusal in the report and they are accordingly referred to the original. We hesitate to use the hackneyed sentence that this report should be in the hands of all workers in malaria, because we fear it is frequently employed without much real meaning, but in the present instance it is so true that no other sentence will take its place.

In addition to the work on malaria tropical typhus occupies about twenty pages of the report, and the enteric fevers, pneumonia, diphtheria, anthrax, leprosy and tuberculosis among the diseases of major importance all receive some attention. When it is added that many bacteria have been studied, observations on vaccine lymph recorded, extract of rice polishings experimented with and a great deal of experimental work on water purification has been carried out, it will be understood that to abstract such a full report *in toto* would be quite impossible. The portion of the report devoted to routine work sheds further light on the activities of the Institute for it includes reports on bacteriology, pathology, water analysis and medico-legal work to mention only some of the subjects dealt with. It is a long time since we have had such a record of activity in our hands and the Director and his staff are to be congratulated for the amount of work they carried out in the year 1931.

ABSTRACTED FROM THE TWENTIETH ANNUAL REPORT OF THE SUPERINTENDING ENGINEER, PUBLIC HEALTH DEPARTMENT, BIHAR AND ORISSA, FOR THE YEAR ENDED 31ST MARCH, 1932

CONSIDERABLE increase in the number and size of waterworks has been made in the last ten years. In 1921-22 there were seven open municipal waterworks in the province, supplying a population of 278,570 with an average daily supply of 2,806,700 gallons. In 1931-32 there were nine open waterworks supplying a population of 477,807 with an average daily supply of 5,550,500 gallons. During the decade there has been an increase of 71.5 per cent in the population provided with a piped supply of water and of 98 per cent in the average daily supply.

Further evidence of the increase in the supply of pure water is given by a comparison of the installations in Government institutions. In 1921-22 there were four institutions with piped supplies of water with a total average daily supply of 81,800 gallons and only one of these supplies was maintained by this department. In 1931-32 there were thirteen institutions with piped supplies with an average daily supply of 519,850 gallons and six institutions with pumping plant for the disposal of sewage. Twelve out of the thirteen water supply installations and all the sewage pumping installations are in the charge of this department.

Still further evidence of progress is given by the steady improvement in the bacteriological purity of the water supplied which now, with one or two exceptions, is not inferior to the standard laid down for public supplies by the Ministry of Health in England.

In every case the improvements in the supplies as regards quantity are due to the work done by this department and in respect of purity to the joint efforts of the two Departments of Public Health and it must be remembered that the present standard will not be maintained, should there be any slackening in the continuous efforts to effect improvement.

Correspondence

ANNUAL REPORT OF THE EUROPEAN AND INDIAN MENTAL HOSPITALS, RANCHI, FOR 1931

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—In the May issue of the *Indian Medical Gazette* you are kind enough to ascribe the 'creed', which I have introduced into the Ranchi European Mental Hospital, as a product of my originality. I regret that I must rebut this impeachment. The idea of a 'creed' for the patients of the Ranchi European Mental Hospital came to me after reading a contribution to volume XV of *Mental Hygiene* by Dr. L. C. Marsh, assistant physician at King's Park State Hospital, Long Island, New York.

Dr. Marsh quotes the 'creed' of the King's Park State Hospital, and, after slightly altering its wording, I adopted it as a 'creed' for the Ranchi European Mental Hospital.

Yours, etc.,

OWEN BERKELEY-HILL,
LIEUTENANT-COLONEL, I.M.S.,
Medical Superintendent.

RANCHI EUROPEAN MENTAL HOSPITAL,
6th June, 1933.

SYPHILITIC IRITIS TREATED BY AN UNQUALIFIED PRACTITIONER

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—The following notes of a case may be of interest to your readers, illustrating as it does the danger of unqualified practitioners:—

B. S., a Hindu male, aged 45 years, came to me with syphilitic iritis. He could not afford a full course of treatment so consulted a *Baid* (an hereditary ophthalmic practitioner). He applied a mixture of lime, washing-soda and a *batika* of his own to the patient's forehead. In three days the forehead was deeply ulcerated and as there was no improvement in his iritis the patient returned to me for treatment, at the end of a week.

Yours, etc.,

J. R. GANGULY, M.B.

GALS,
BURDWAN DISTRICT,
25th April, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL E. H. V. HODGE is appointed as Civil Surgeon, Dacca, *vice* Lieutenant-Colonel C. R. O'Brien.

Lieutenant-Colonel B. F. Eminson, Civil Surgeon, Dharwar, to be Civil Surgeon, Hyderabad (Sind), with attached duties.

Lieutenant-Colonel M. J. Holgate, O.B.E., Civil Surgeon, Hyderabad (Sind), to be Civil Surgeon, Karachi, *vice* Lieutenant-Colonel I. D. Jones, proceeding on leave pending retirement.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's Personal Staff, with effect from the date of assumption of charge:—

To be officiating surgeon

Major W. R. Stewart, *vice* Captain (local Major) F. M. Collins granted leave ex-India.

Major J. C. Pyper, an Agency Surgeon, is posted as Residency Surgeon, Kashmir, with effect from the forenoon of the 4th May, 1933.

Major A. Y. Dabholkar, M.C., Assistant Director of Public Health, Northern Registration District, Ahmedabad, is transferred to Poona as Assistant Director of Public Health, Central Registration District, and placed in charge of the office of the Director of Public Health for the Government of Bombay, in addition to his own duties, as a temporary measure, pending further orders.

The services of Major A. C. Chatterjee are placed temporarily at the disposal of the Chief Commissioner, Delhi, for appointment as Assistant Director of Public Health, Delhi, with effect from the date on which he assumes charge of his duties.

Major C. M. Ganapathy, M.C., is appointed to officiate as Deputy Director-General, Indian Medical Service, with effect from the 19th May, 1933, *vice* Lieutenant-Colonel A. J. H. Russell, C.B.E., granted leave.

The services of Captain F. R. W. K. Allen are placed temporarily at the disposal of the Government of the Central Provinces, with effect from the date on which he assumes charge of his duties.

To be Lieutenants (on probation). 4th April, 1933

J. White, H. A. Ledger, T. F. O'Donnell, F. C. Leach, W. W. Laughland.

LEAVE

Lieutenant-Colonel A. J. H. Russell, C.B.E., Officiating Deputy Director-General, Indian Medical Service, is granted leave on average pay for 1 month and 5 days, with effect from the 12th May, 1933, combined with leave on half average pay for 2 months and 2 days.

Lieutenant-Colonel R. B. Lloyd, Imperial Serologist, is granted leave on half average pay, with effect from the 18th April, 1933, up to and including the 22nd September, 1933. He is permitted to prefix the holidays from the 13th to 17th April and to affix the recognized Pujah holidays to the leave.

Lieutenant-Colonel C. R. O'Brien, Civil Surgeon, Dacca, is allowed leave from the date of availing up to the 3rd April, 1934, namely, leave on average pay for 3 months and 4 days, and leave on half average pay for the remaining period.

Lieutenant-Colonel I. D. Jones, Civil Surgeon, Karachi, is granted leave on average pay for 1 month and 14 days followed by leave on half average pay up to 8th September, 1934, inclusive, preparatory to retirement, with effect from 31st March, 1933.

Major T. H. Thomas, Civil Surgeon, Mymensingh, is allowed leave for 6 weeks, with effect from the 16th May, 1933, or the date of availing.

PROMOTIONS

Lieutenant-Colonel to be Colonel

C. I. Brierley, C.I.E., dated the 17th February, 1933, with seniority from 28th February, 1927.

Brevet-Colonel C. A. Gill, K.H.S. Dated 28th February, 1933, with seniority 3rd June, 1922.

Captain (on prob.) W. Aitchison, M.C., to be Major (Prov.) (on prob.), 20th December, 1932.

Lieutenant to be Captain (provisional)

D. McCarthy, dated 22nd April, 1933.

RETIREMENTS

Lieutenant-Colonel R. F. Steel retires 28th April, 1933.

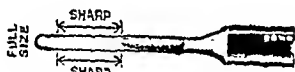
Lieutenant-Colonel H. P. Cook retires 28th February, 1933.

Notes.

A NEW ANTERIOR SYNECHIA KNIFE

By C. V. KRISHNASWAMI, M.R., B.S., D.O.M.S.,
F.R.C.S. (Edin.)

In cases where three-quarters or more of the pupil is incarcerated in a corneal scar and as a consequence the anterior chamber to a corresponding extent is very shallow or practically non-existent, I have experienced a great deal of difficulty in insinuating the ordinary instruments recommended for the release operation, like a Graefe's or Herbert's knife or Ziegler's knife-needle, since the sharp point either pierces the cornea or gets entangled in the iris. To obviate this difficulty I use a special knife made for me by Messrs. Down Bros., Ltd., London, the details of which are clearly shown in the illustration.



An ordinary keratome incision is made at a spot where the anterior chamber is deepest and of a size slightly larger than the width of the blade of the instrument, with the usual precautions for avoiding loss of aqueous. The instrument is then introduced through the incision until the point is well past the site of adhesion. By either depressing the handle or by a series of sawing movements the adhesion is severed. Sometimes the iris is only partly cut through, some of the fibres simply stretching before the instrument without giving way. When this occurs the instrument is partly withdrawn, pushed past the scar on the opposite side and again made to cut the iris as before. Being double-edged the instrument is used with equal facility with either hand and made to cut in either direction. The point being blunt, as are also the edges down to three millimetres from the tip, no damage to the cornea or the iris occurs.

I have operated on over fifteen cases and the instrument has served my purpose extremely well.

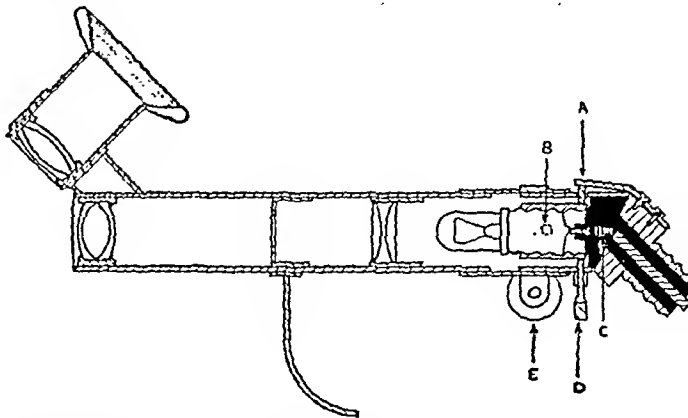
A HAND SLIT LAMP

By N. BISHOP HARMAN, F.R.C.S.

The value of the standard forms of slit lamps for certain ophthalmic investigations is undoubted. But the immobility of these large instruments limits their use to the consulting room and clinic.

The hand slit lamp shown has been devised with the intent of securing an instrument that could be used as readily and as easily as an electric ophthalmoscope; so that it can be carried about, and used with ease for the examination of children, and patients in bed or in their own homes. It cannot, by reason of its small size, compete with the large instruments in magnification and in resolution of fine detail. Yet it will secure a valuable view of the media of the eye as deep as the anterior part of the vitreous. The small lamp as compared with the large might be said to have

something like the relation of the two-thirds inch objective of the microscope to the one-sixth inch objective. But the small lamp gives the same effect of depth as the large lamp, so that its value for localization is certain.



In the diagram, A represents the spring and D the screw controlling the lamp centre. B indicates the position of the trunnion, C the centre contact of the lamp, and E the clamping screw. Note that in practice the filament and slit are horizontal.

The lamp is fitted to the battery handle of an electric ophthalmoscope; or a small adapter can be supplied with leads to a torch battery or other suitable source of current. At the upper end, set at right angles to the ophthalmoscope handle, is an eyepiece consisting of a triple achromatic lens giving a linear magnification of 12 X. The lens holder is so made that other powered lenses can be substituted. The case of the eyepiece is graven with a scale so that the focus of the lens, once found, can always be recovered.

Below the eyepiece, and at an angle of 45° to it, is the projection combination, forming a horizontal slit of light at a distance of one inch. It comprises a gas-filled lamp with a single strand filament, made for two cell or three cell dry batteries. The centre pole of the lamp abuts on to a spring contact, so that all lamps can be set with the filament horizontal. A powerful condensing system produces an image of the filament upon a slit fixed in the tube, so that the projection lens, an achromatic lens of some 60 dioptries, can form a clear image of this slit, free from disturbing haze or filament irregularities.

In use, the instrument must be kept steady in relation to the eye of the patient, and yet allow focusing for depth. This can be obtained by the following manoeuvre. The lamp is held by the main tube with the battery handle or adapter hanging down. There is a trigger-like spur projecting below the main tube, and this lies conveniently between the second and third fingers. The thumb rests on the top of the tube, with its end in the angle between the tube and eyepiece, the forefinger lies along the side, so that the projecting tip of the finger can rest against the patient's cheek at the lower border of the orbit. This contact gives steady support. Alternate crooking and straightening the forefinger brings the lamp nearer or further from the eye and gives focusing for depth.

Adjustments of the instrument are of the fewest, normally the eyepiece alone is likely to require setting. But the setting of the lamp bulb, in case of replacement, needs attention. The filament must be horizontal, and in the axis of the system. Whether or no this adjustment is correct, can be seen by looking at the face of the projection lens. The bright line of light should cut the lens horizontally into two equal parts. If this line is not true, the position of the filament must be altered. The lamp mount is pivoted at its front end on a horizontal axis on trunnions. At the back there are a screw and a spring on a vertical axis, the one lifting the back, the other allowing it to fall.

As the back rises, so the filament is lowered, and *vice versa*, the movement being made by releasing or screwing in the lower screw. The distance between the lamp and the condenser system can be varied by loosening the large headed screw under the lamp end of the tube, and allowing the tube to slide over the lamp stem a little. This large headed screw should be turned firmly when the adjustment has been made. Once the adjustment is obtained, it need not be altered until a new lamp is required.

It is better not to wear spectacles when using the lamp so that one's eye can be well within the shield of the ocular. It is well not to overrun the electric bulb, so when a new battery is used the switch to the rheostat should be turned on no more than two-thirds until the battery weakens.

The hand slit lamp is made by Messrs. Rayner of New Bond Street, London.

DEFORMITIES OF THE TOES

DR. STRACKER discusses the different forms of toe-deformities, their ætiology and their treatment. In cases of chronic inflammation of the joint of the great toe, the author discusses the possibility of this condition being easily mistaken for arthritis. For its treatment he recommends massage and diathermy, and internally urecidin. In acute onset, local antiphlogistic treatment with Antiphlogistine proved of great value. To lessen the pain when walking, it is recommended that two strips of wood, placed at right angles, be attached to the sole of the shoe in the area of the ball.

Priv. Doz. Oskar Stracker in the *Wiener Klinische Wochenschrift*.

AN INTRODUCTION TO X-RAY PHOTOGRAPHY

We have received from the Agfa Photo Company a very useful book entitled *An Introduction to X-Ray Photography*, by Professor John Eggert. The book deals with its subject in a general way and does not lay any undue emphasis on the products of the firm who are responsible for its publication.

The first few pages in the book are devoted to a subject of very great historical interest, namely, the reproduction of Röntgen's original paper on 'a new kind of rays', published first in 1895. There then follows a chapter on the theoretical side of the subject. This is well written and, what is more important to most readers in this country, it is well translated. The diagrams are useful and make the text easy to understand. X-ray workers will find it very helpful. The main portion of the book is devoted to the practical application of x-rays, and here technical details are described very lucidly.

We can recommend this as a very valuable and interesting publication. The Agfa Company have asked us to announce that they will be very pleased to give a free copy of the book to anyone interested in the subject who will apply to their Bombay office, Canada Building, Hornby Road.

THE MAINTENANCE OF NUTRITION

At the Thirty-sixth Annual General Meeting of Bovril, Ltd., which was held in London, on 3rd March, 1933, with the Lord Luke, K.B.E. (the Chairman), presiding, Sir James Crichton-Browne, M.D., LL.D., F.R.S., said that he did not wish to pose as monumental, but he thought he could claim to be an impressive example of what steadfast allegiance to Bovril could do, both in the maintenance of nutrition, and the prevention of obesity.

They were told by all those who ought to know that what was wanted above all things at the present moment was confidence. The Prime Minister had diagnosed the condition from which so many people were suffering as being in a state below par.

Sir James believed Bovril was well qualified to assist in correcting and alleviating that condition. Bovril braced up the nerves and imparted spirit and confidence, as was conspicuously shown in the greivous influenza epidemic through which the country had just passed. The enormous and progressive demand for Bovril during the epidemic was conclusive proof of the confidence felt in it by the people. They had proved for themselves, on the large scale, that the timely use of Bovril increased resistance to the inroads of influenza, that it afforded support during an attack, and that it was restorative in the debility—often protracted and hazardous—that followed in its train.

NEW HYPNOTIC PRODUCTS

BURROUGHS WELLCOME & Co., Snow Hill Buildings, London, E.C., have added to their list the following three hypnotic products:—'Tabloid' Phenobarbitone, gr. 1, 'Tabloid' Phenobarbitone Soluble, gr. 1, 'Tabloid' Barbitone Soluble, gr. 5. These products are issued in bottles of 25 and 100.

The two 'Tabloid' phenobarbitone products are of special value in the treatment of epilepsy and aural vertigo. They are also helpful in insomnia and nervous conditions and states of nervous excitement.

'Tabloid' Barbitone Soluble is more rapid in action than ordinary barbitone, which is one of the most effective hypnotics of the ureide series.

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Communications for the Publishers relating to Subscriptions and Advertisements should be addressed to THE PUBLISHERS, *The Indian Medical Gazette*, P. O. Box No. 54, Calcutta.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with re: diagnoses, etc., nor can they name practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

ATEBRIN IN THE TREATMENT OF INDIAN STRAINS OF MALARIA

By R. N. CHOPRA, M.A., M.D. (Cantab.)

LIEUTENANT-COLONEL, I.M.S.

Professor of Pharmacology

BIRAJ MOHAN DAS GUPTA, L.M.P.

Officiating Professor of Protozoology

and

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FROM the time of the discovery of cinchona up to a few years ago, cinchona bark and the alkaloids obtained from it, particularly quinine, were the only drugs that had been used effectively in the treatment of malarial fevers. These alkaloids, although effective in many respects, are very bitter in taste, have to be given in fairly large quantities, and produce unpleasant by-effects. Besides this, although they destroy the asexual forms of different malarial parasites, they unfortunately have little effect on the sexual forms and no effect whatsoever on the gametocytes of the malignant tertian parasite. In quartan malaria their effect, even on the schizonts, is less powerful and they sometimes fail to relieve the paroxysms. Many other remedies have been introduced from time to time, but none of these have proved effective. The shortage of quinine was especially felt during the Great War and research with the object of finding a synthetic drug that could be used in its place was considerably stimulated. It was therefore a great event when, in 1926, a synthetic compound known as plasmochin (or plasmoquine) was discovered by Professor Schulemann of the Bayer-Meister Lucius research laboratories at Elberfeld. Chemically, this preparation is an amino-quinoline derivative in which a basic aliphatic radicle is united to a quinoline nucleus by a connecting link of nitrogen. This drug could be given in very small doses and has not a very bitter taste. It was at first thought to have a definite curative effect in the treatment of all forms of malaria, but later experience showed that while it was effective in curing benign tertian and quartan malaria, by itself in sub-tertian it was of no therapeutic value because it had no action on the schizonts, and some observers went so far as to say it had a provocative action. It however possessed the remarkable and unique property of destroying the crescents in the peripheral blood. In this type of malaria therefore it was still necessary to use quinine, in fact the two drugs were combined, the quinine for the schizonts and

plasmoquine for destroying the crescents, to prevent the patient from acting as a source of infection.

Although the cure of benign tertian and quartan malaria is brought about more effectively by plasmochin than by quinine, the tendency is, in order to obtain the maximum effects, to treat even these two infections with a combination of quinine and plasmochin—quino-plasmochin as it is called. With the two drugs together the relapse rate in benign tertian infections is said to be reduced from the usual 50 per cent to 3 per cent. Plasmochin is also said to have an undoubted prophylactic value whereas quinine has none. With all these qualities, however, it is very toxic and may give rise to severe toxic symptoms and for this reason it is advisable that it should be taken under medical supervision.

Schulemann and his collaborators therefore continued the work with renewed energy towards finding a more effective anti-malarial remedy, and in 1929 synthesized atebrin which originally they called 'erion'. Chemically this preparation is the di-hydrochloride of an alkylamino-alkylamino-acridine derivative. It is a yellow powder with a bitter taste, soluble to 7 per cent in water at 40°C., and like quinine it shows fluorescence under ultra-violet radiation. Since its introduction it has been extensively tried by a large number of workers in every part of the world with good results. This drug is now being largely used by medical practitioners in India, but its detailed effects on the Indian strains of malarial parasites have not been fully investigated, although Napier and Das Gupta (1932), Napier, Butcher and Das Gupta (1932) and Knowles and Das Gupta (1932) carried out detailed studies regarding its action on a small series of cases.

It has been recently shown by James (1932) and others that the action of anti-malarial drugs varies a great deal with different strains of parasites occurring in different parts of the world. James' Madagascar strain failed to react to quino-plasmochin in the same way as other strains, and there are many other examples.

In view of the fact that atebrin is beginning to be considered as effective as quinine and its use is likely to be considerably extended in this country, we took up a detailed study of the effects produced by it in a series of patients in the Carmichael Hospital for Tropical Diseases. In Bengal, malaria is endemic and in certain parts a very virulent type of malignant tertian malaria is prevalent. Our patients came from different parts of the province and probably represented many strains of parasite prevalent here. In this paper we have briefly summarized the results we have obtained by treatment of malaria with this drug. Extensive chemotherapeutic studies have also been carried out on monkey malaria, but these results will be presented in a separate paper.

The studies in connection with human malaria were mainly undertaken to determine :—

(a) The effects of the drug on the temperature and other symptoms met with in the disease.

(b) Its effects on the sexual and asexual forms of the parasites, and time taken for their disappearance from the peripheral blood.

(c) Its effect on the splenic enlargement and relapses.

(d) The effect of the drug on the pulse rate, blood pressure, respiration, and generally on the patients, and its excretion from the body.

(e) Any untoward effects produced by its administration.

The patients suffering from malaria were admitted under the senior author (R. N. C.) and a thorough physical examination was conducted immediately after admission. The peripheral blood was examined and the number of parasites, both sexual and asexual, per cubic centimetre was determined. Except in urgent cases the anti-malarial treatment was not started until the parasitic counts were fairly constant for two or three consecutive days. The pulse, blood pressure and respiration were carefully recorded. In the meantime the patients were put on a simple alkaline mixture. Daily counts of parasites in the peripheral blood during this period enabled us to watch the progress of the cases and gave us information regarding the intensity of the infection. If the parasites in the peripheral blood were scanty, these were allowed to increase till the count was fairly high, and rigors and other symptoms were produced, before the drug was administered. Atebrin was given by the mouth in tablet form, one tablet containing 0.100 gramme being given three times a day for five consecutive days. No other drug was given except a light purgative whenever necessary. No restrictions regarding diet were observed. Careful daily parasite counts were made while the drug was being administered in one series of 18 patients, but in another series of 20 cases only a rough estimation of the number of parasites in the peripheral blood was made daily.

After completion of the course the patients were carefully observed in the hospital for a fortnight, daily examinations of the blood for parasites and parasitic counts being made. If the thick and thin films were negative, in suspicious cases cultural examinations of the blood for malarial parasites were always made. In addition to the cases reported here in detail, atebrin was given to a number of out-patients and it was on these that some of the by-effects reported below were noted.

In table I the details of 18 cases are given. A study of this table will show that cases of acute infection of all three forms of malaria and some of the relapsing cases, all responded equally well to this drug. Usually the temperature begins to settle down on the second or third day of treatment and on the fourth day

there is complete disappearance of the parasites from the peripheral blood. Rigors are seldom observed after the third day of administration of atebrin. In mild cases of benign tertian infections if atebrin treatment is started on the day of the rigor, the next rigor is sometimes manifested in the form of a chilly sensation only, and in cases infected with the quartan type it does not come at all. In relapsing cases the temperature takes longer to settle down than in acute fresh infections.

A study of the table will show that the action of atebrin on the asexual forms of the parasites is gradual and not so rapid as that of quinine. It generally takes 0.6 to 0.9 gramme of the drug (*i.e.*, the administration of 3 tablets for 2 or 3 days) before the asexual forms of benign tertian disappear from the peripheral circulation. Its action on the quartan parasites is as powerful as on the benign tertian (*vide* cases 12, 13, 15 and 17). On the asexual forms of malignant tertian parasites atebrin appears to act just as readily as on the schizonts of benign tertian.

As regards the sexual forms—gametocytes—these were much more slowly acted upon than the asexual forms, the action being marked on the benign tertian and quartan gametocytes, but absent in the case of the malignant tertian gametocytes, as is the case with quinine. That the drug had no effect whatsoever on the sexual forms of malignant tertian parasites—crescents—is clearly indicated by their persistence in cases 2, 4, 9 and 10 after a full course of treatment with the drug. That the drug adversely affected the sexual forms of benign tertian and quartan parasites is obvious from a number of cases in which definite evidence of degeneration could be detected in the gametocytes.

Patient no. 8 was a young child; he vomited his first dose of atebrin, but the drug was continued and he apparently retained the later doses. The fever fell to normal after 60 hours, but subsequently rose again daily to 99° or 99.4°F.; scanty parasites also persisted.

Patient no. 9 is of special interest as he had a very high parasite count and was in danger of going on to the pernicious type. An intravenous injection of 0.1 gramme of atebrin dissolved in 1 cubic centimetre of distilled water was given at once as well as a tablet by the mouth; this was repeated on the two following days. The asexual parasites rapidly decreased in number and the temperature came down. No untoward effects were observed after intravenous administration of the drug and it would appear that the action is more rapid when given by this route.

Patient no. 10 had a mixed infection with benign tertian and malignant tertian and responded to the treatment less readily than in the case of single infections, the schizonts persisting for four days after the administration of atebrin.

Patient no. 11 was treated in the hospital for benign tertian malaria with atebrin 3 months ago, and came in with a fresh malignant tertian infection.

The observations recorded above were corroborated by results obtained in a further series of 20 cases details of which are given in table II. In this series it was not possible to enumerate the parasites daily as in the series given

TABLE I

No.	Race, sex and age	Recent treatment given or not	PARASITE, PARASITE COUNT PER CMM. AND TEMPERATURE BEFORE TREATMENT				PARASITE COUNT AND TEMPERATURE DURING AND AFTER TREATMENT								Days of fever	REMARKS
			Species	Asexual	Sexual	Temp. F.	2ND DAY		3RD DAY		4TH DAY		5TH DAY			
							Asex.	Sex.	Asex.	Sex.	Asex.	Sex.	Asex.	Sex.		
1	E. M., 50	Yes	B. T.	9,840	180	102.8	6,240	240	1,780	640	0	40	0	0	2	Crescents persisted.
2	H. M., 27	Yes	M. T.	9,240	0	103.4	240	0	840	Sc.	0	100	0	80	3	
3	H. M., 20	No	B. T.	16,340	480	102	9,900	340	800	80	0	0	0	0	2	
4	M. M., 22	No	M. T.	2,400	1,400	100.2	0	Sc.	0	Sc.	3	Do.
5	H. M., 16	No	B. T.	30,000		104.6	5,200		0	0	0	0	0	0	2	Absconded.
6	H. M., 40	No	M. T.	8,800	0	99	6,400	0	
7	M. M., 30	No	B. T.	28,000		100.4	0	2	
8	I. Ch. M., 7	No	M. T.	14,200	0	..	Sc.	7	Crescents persisted.
9	I. Ch. M., 18	No	M. T.	128,000	0	105	0	Sc.	0	Sc.	0	Sc.	..	
10	A. I. M., 20	No	B. T. and M. T.	98,000	1,800	105	15,700	2,400	1,600	1,840	1,020	2,400	0	2,000	4	
11	H. M., 14	Yes	M. T.	12,560	440	104	2,900	480	0	884	0	Sc.	0	Sc.	2	Do.
12	H. F., 18	No	Q.	3,520		100.2	1,440		880	..	0	0	3	
13	H. M., 22	No	Q.	1,000		98	560		80	..	0	0	3	
14	A. I. M., 26	No	B. T.	21,400	0	100	10,000	Sc.	Sc.	0	0	0	0	0	2	2
15	H. F., 18	No	Q.	800		98	420		0	0	0	0	0	0	2	
16	M. M., 35	Yes	B. T.	9,840	0	103	1,200		0	0	0	0	0	0	2	
17	H. M., 27	No	Q.	2,400	0	103	Sc.		Sc.	0	0	0	0	0	2	2
18	M. M., 27	No	B. T.	10,000		104	0	Sc.	0	V. Sc.	0	0	0	0	2	

For abbreviations used see table III.

TABLE II

No.	Race, sex and age	Recent treatment given or not	FINDINGS BEFORE TREATMENT				FINDINGS DURING AND AFTER TREATMENT										Days of fever	REMARKS
			Species	Asexual	Sexual	Temp. F.	2ND DAY		3RD DAY		4TH DAY		5TH DAY					
							Asex.	Sex.	Asex.	Sex.	Asex.	Sex.	Asex.	Sex.				
1	H. M., 18	No	B. T. and M. T.	+, So.	+, Sc.	103°/98°	Sc.	Sc.	V. Sc.	Crescents.	0	Crescents.	0	Sc.	3			
2	M. M., 19	Yes	B. T. and M. T.	+	0	..	+	0	Sc.	0	0	0	0	0	0	3		
3	E. M., 30	Yes	M. T.	Sc.	0	99°	Sc.	0	0	0	0	0	0	0	0	2	Two courses.	
4	A. I. F., 21	No	B. T.	V. Sc.	0	..	V. Sc.	0	0	0	0	0	0	0	0	2		
5	A. I. M., 11	Yes	B. T.	Sc.	0	99°	Sc.	Sc.	0	0	0	0	0	0	0	2		
6	E. M., 56	No	M. T.	+	0	101.4°	Sc.	0	Sc.	0	0	0	0	0	0	3	See note.	
7	A. I. F., 48	Yes	M. T.	+	..	102°	Sc.	—	Sc.	—	Sc.	0	0	0	0	2		
8	H. M., 18	No	B. T.	+	+	104.4°	Sc.	Sc.	0	0	0	0	0	0	0	3		
9	H. M., 13	No	M. T.	+	+	103.6°	Sc.	Sc.	0	0	0	0	0	0	0	2	Two courses.	
10	H. M., 35	No	M. T.	+	0	102°	Sc.	0	0	Sc.	0	Sc.	0	Sc.	0	2		
11	E. M., 25	Yes	M. T.	+	0	103°	+	0	Sc.	0	0	0	0	0	0	2	Two courses.	
12	H. M., 9	No	M. T.	+	960	102.8°	Sc.	++	Sc.	+	0	+	0	+	0	3		
13	H. M., 11	No	M. T.	+	0	99°	Sc.	Sc.	V. Sc.	Sc.	0	Sc.	0	Sc.	0	7		
14	H. F., 32	No	Q.	+	Sc.	100.6°	Sc.	Sc.	Sc.	Sc.	0	Sc.	0	0	0	2		
15	I. Ch. M., 20	No	M. T.	+	+	103.6°	Sc.	+	V. Sc.	Sc.	0	Sc.	0	So.	0	2		
16	H. M., 18	No	B. T.	++	+	104°	+	+	Sc.	+	0	0	0	0	0	2		
17	H. F., 21	No	M. T.	+	0	103°	Sc.	0	Sc.	0	0	0	0	0	0	2		
18	H. M., 11	No	M. T.	+	0	102.2°	Sc.	0	Sc.	0	0	0	0	0	0	2		
19	M. M., 30	No	M. T.	Sc.	0	100°	Sc.	0	Sc.	0	0	0	0	0	0	3		
20	M. M., 35	No	M. T.	Sc.	0	101°	Sc.	0	0	0	0	0	0	0	0	3		

For abbreviations used see table III.

in table I. The blood was carefully examined daily in every other respect, but only a rough estimate of the number of parasites in the peripheral blood was made. These cases were mostly of the acute type resembling the first series and they reacted in more or less the same way to atebirin.

Cases 3 and 9 in this series are worthy of note. Although the infections were not heavy, these patients did not react to the ordinary five days course of atebirin and very scanty malignant tertian rings could still be detected after the course. A second course of atebirin was given and with it the symptoms subsided and the parasites disappeared from the peripheral circulation. Patient no. 3 improved but left the hospital of his own accord after the second course before his blood could be finally examined. In patient no. 9, the temperature persisted after one course of treatment but subsided after the second course of two tablets twice daily for four days. In patient no. 11 benign tertian rings and trophozoites persisted after a 5-day course of atebirin. The patient was also given a second course but left the hospital before completion of the course. Such cases are difficult to explain. The possible explanation may be that in a low degree of pyrexia the parasites lodge themselves in the internal organs (only a few remaining in the peripheral blood) and are thus less readily acted upon by the drug. In cases 1, 10, 12, 13 and 15 crescents persisted after a full course of atebirin but 0.01 gramme of plasmochin twice daily for two days produced their disappearance. Patient no. 6 felt very depressed and his general condition was low after four days administration of the drug and for two days he had to be put on diffusible stimulants. A number of other patients in the two series complained of a feeling of depression and turned yellowish in colour, but this did not amount to anything serious.

In table III we have put all the chronic cases of malaria with enlargement of spleen which were treated with atebirin. In all these patients besides the usual examinations carried out in the first two series, very careful records were kept of the variations in the size of the spleen, with the treatment. Besides this the effects of the drug on the temperature have been included in the table. A study of this table will show that there was rapid reduction in the size of the spleen to practically its normal size in every case of acute infection. In long-standing cases where the spleen was hard the decrease in size was more gradual and the organ often did not come back to its normal size.

As regards the temperature, it will be seen that the chronic cases did not react so readily to atebirin treatment as the acute cases. In patient no. 3, the temperature persisted even on the 8th day and a second course of atebirin was necessary to bring it down. In patients nos. 4, 5, and 14 the temperature persisted after four days of treatment.

Relapses.—It has been urged that the most valuable property of atebirin is its power to prevent relapses and many workers have borne testimony to this effect. But in our experience quite a number of patients, at least five out of a series of 39, apparently relapsed. It must be pointed out however that, in a malaria endemic area such as this, it is very difficult to be certain whether these were fresh infections or

relapses. Two patients relapsed while they were actually under observation in the hospital after the course and parasites of the same species were found in the peripheral blood. (A number of relapses were also reported in the patients treated outside the hospital.) Even though these may not be real relapses but fresh infections, it may be noted that infection took place before the atebirin had been fully excreted from the body of the individual. Although in an endemic area like this, it is difficult to prove in the human patients that relapses actually did occur after a course of atebirin, we have ample evidence in experimental malaria in monkeys (*M. mulatta*) that the drug does not eradicate infection from the body and that relapses are common. In quite a number of these animals after a course of the drug and disappearance of symptoms and parasites from the peripheral circulation, the parasite reappeared usually within two weeks and the animal showed symptoms of the disease.

Prophylactic uses.—Atebrin is claimed to have prophylactic properties and has been used by some workers for this purpose with good results. It is said to have been continued for months without producing any untoward effects in doses of 0.1 gramme daily. It has also been combined with plasmochin for this purpose, 0.1 gramme of atebirin and plasmochin 0.001 gramme being given together daily. The prophylactic value of atebirin is still under investigation, but so far as we can see it has no more true prophylactic action than the cinchona alkaloids.

Blackwater fever.—Atebrin can be given to patients suffering from blackwater fever without ill-effects. It can also be given to patients who are sensitive to quinine and in whom administration of quinine produces hæmoglobinuria.

Pulse rate, blood pressure, respiration, etc.—In a series of nine patients the effects of atebirin on the blood pressure, pulse rate and respiration were recorded. Careful records of these were obtained for a few days preceding the administration of the drug and these were compared with those obtained both when the patients were actually taking atebirin and a few days after the cessation of the drug. So far as possible the readings were taken under exactly the same conditions and at a particular time of the day with due regard to food, posture, temperature, etc.

So far as the blood pressure (systolic and diastolic) is concerned there was a slight lowering varying from 5 to 12 millimetres of mercury in some patients. In others there was no change whatsoever. The pulse rate and respiration also showed no appreciable changes when the patients were under the effect of the drug. From these results one is justified in concluding that atebirin has little, if any, depressing effect on the cardio-vascular system.

TABLE III

Number	Race, sex and age	Duration	SPLEEN IN INCHES BELOW COSTAL MARGIN AND TEMPERATURE BEFORE, DURING AND AFTER TREATMENT.							REMARKS
			Before treatment	1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day	After treatment
1	H. M., 18	3 months	1½	100°/98.4°	99.8°/98°	98.4°/97°	Afebrile	Afebrile	Afebrile	—
2	H. M., 11	6 "	1½	99°/98.4°	98.8°/98°	98.4°/97°	"	"	"	P
3	H. M., 13	6 "	3	103.6°/102°	102.6°/99°	98.2°/97.6°	"	"	"	P
4	H. M., 9	1 year	U	98°	98.4°/98°	99.2°/97.6°	99°/98°	98.8°/98°	98.8°/98°	1
5	H. F., 32	3 years	1½	100.6°/98°	98.6°/97°	99.4°/98°	98.4°/97.8°	98.8°/98°	99°/98°	P
6	H. F., 20	6 days	P	98.4°	101.8°	99°	98°	Afebrile	Afebrile	—
7	H. M., 35	5 years	4	101°	99°	98.8°	97.8°	98°	98°	2
8	H. M., 22	2 months	3	102.8°	101.6°	98.4°	Afebrile	Afebrile	Afebrile	1
9	I. Ch. M., 7	5 days	2½	104°	104°	101°	99.4°	99°	99.6°	P
10	I. Ch. M., 20	3 months	2	103.6°/100.2°	101°/98°	98°/97°	Afebrile	Afebrile	Afebrile	P
11	H. M., 27	1 year	U	104.2°/101.6°	100°/97.6°	98.4°/97°	"	"	"	1
12	H. F., 30	6 months	3	103°/100.4°	100°/98°	98°/97°	"	"	"	1
13	H. F., 48	1½ "	1	102.4°	99.2°/98°	98°/97°	99°/98.4°	"	"	P
14	A. I. F., 21	1 year	1½	102°/98.4°	100°/98.4°	99°/98°	99°/98.4°	"	"	P
15	H. F., 19	1½ years	1	103°/98.4°	100.4°/99°	101°/99.4°	99°/97.8°	"	"	P
16	M. M., 30	3 days	P	104°/98°	101.6°/98°	98.4°/97°	Afebrile	"	"	—
17	M. M., 25	3 months	P	98.4°	100°	Afebrile	"	"	"	—
18	E. M., 21	2 "	P	102°	101°	99°	"	"	"	P
19	A. I. F., 21	3 years	½	102.8°	101°	Afebrile	"	"	"	P
20	H. M., 27	3 weeks	P	103°	103°	"	"	"	"	—
21	A. I. M., 26	3 years	P	103°	99.8°	Afebrile	"	Afebrile	"	—
22	H. F., 18	2 years	2	100.2°	98.8°	99°	"	"	"	—
23	M. M., 35	5 months	1½	102°	98.4°	97.4°	"	"	"	—
24	A. I. M., 11	1 month	P	99°	98.4°	100°/98°	"	"	"	—
25	M. M., 27	7 days	P	104°	98.6°/97.6°	100°/98°	"	"	"	—
26	H. M., 24	10 months	3	102°	101°/98°	100°/98°	"	"	"	1
	H. M.	2 "	½	103°/98°	99°/98°	100°/98°	"	"	"	—

Abbreviations used:—

E. = European. A. I. = Anglo-Indian. H. = Hindu. M. = Mohammedan or Male. F. = Female. I. Ch. = Indian Christian. B. T. = Benign tertian. M. T. = Malignant tertian. Q. = Quartan. + = Moderate infection. ++ = Heavy infection. Sc. = Scanty. V. Sc. = Very scanty. 0 = No parasites found. P = palpable. U = Down to umbilicus.

in the majority of the patients. We have given the drug to patients suffering from endocarditis and myocarditis without ill-effects.

Excretion.—In a series of patients we worked out the excretion of the drug. The drug is mostly excreted by the kidney and its presence can be roughly detected in the urine by production of the characteristic yellow colour on addition of an acid. The test suggested by the makers is to extract the alkalinized urine with ether, and dissolve the residue resulting from the evaporation of ether extract in strong sulphuric acid, when a yellow colour appears. This latter test is more accurate, and we actually used a modification of it. The urine was first treated with lead acetate to remove all other matter and the lead was removed from the filtrate by the addition of ammonium sulphate. The filtrate was then extracted with ether and tested with acid in the ordinary way. The drug appears in the urine on the second day after administration and can be detected up to 15 or 20 days or even longer. The excretion is not regular and may stop for a day or two and then reappear. Our observations on Indian patients confirm the view that there is some tendency towards cumulation of the drug in the body. Atebrin undoubtedly persists in the body for a much longer period than quinine or plasmochin. If excretion is hindered there is a tendency for the appearance of the dye in the skin which assumes a yellowish tinge.

Untoward and toxic effects.—Atebrin unlike plasmochin is not a very toxic drug. Double the usual dose of 0.3 gramme per day (i.e., 0.6 gramme in 24 hours) can be tolerated, but larger doses may produce gastro-intestinal irritation. In spite of the tendency referred to above of cumulation of the drug in the system we gave two 5-day courses of the drug with a few days interval between without producing any toxic effects, and with therapeutic benefit. Some patients complained of slight pain or a sensation of uneasiness in the epigastric region soon after taking the drug. This generally started on the second or third day and persisted as long as the drug was being administered. The pain was never so severe as that produced by plasmochin. In none of our series did we get the severe abdominal pains described by Green (1932). A number of our patients complained of headache and loss of appetite while the drug was being given, but this also passed off when atebrin was stopped. In some patients a profound feeling of general depression started on the third day of treatment and persisted for several days after the drug was stopped. The patient felt as if he had 'no life in him' and had no desire to make physical exertion and wished to remain lying down. In some of the patients diarrhoea was produced on the second and third days of treatment and persisted while the drug was being given. The diarrhoea was of a mild type and no particular treatment was necessary. It stopped with the cessation of the

drug. In a few patients, especially those who were obese, palpitation occurred which was quite distressing but stopped when the drug was discontinued and in one patient cardiazol had to be administered. In one case mental disturbances were reported to have occurred.

A yellow staining of the skin and conjunctiva occurred in several of our patients, but the coloration as a rule was very slight and in none of the patients did it amount to a jaundice-like appearance.

Summary and conclusions

From a study of this series of patients one can draw the following conclusions:—

(1) Atebrin is an effective drug in the treatment of Indian strains of malaria. Its destructive action on the asexual forms of benign tertian, malignant tertian, and quartan types of malaria is about equal, the schizonts disappearing from the peripheral circulation after 0.6 to 0.9 gramme of the drug, i.e., the administration of 3 tablets of 0.1 gramme for 2 or 3 days.

(2) The sexual forms or gametocytes are more slowly acted upon than the asexual forms. The gametocytes of the benign tertian and quartan types are readily destroyed and degenerative changes can be observed in them shortly after the administration of the drug is started. The gametocytes of the malignant tertian type—i.e., crescents—are not touched at all.

(3) The drug is effective in doses of 0.1 gramme three times a day, the course lasting for five days, making a total of 1.5 gramme of the drug for the cure. In the majority of patients such a course is effective, but in a few of the persistent ones it may have to be repeated after a few days interval. The drug can also be effectively given intravenously in doses of 0.1 gramme dissolved in 1 to 2 cubic centimetres of distilled water when the number of parasites in the peripheral blood is large.

(4) In chronic types of malaria the drug is effective and produces a rapid reduction in the size of the spleen.

(5) Atebrin is reported to prevent relapses, but the evidence at our disposal shows that this is not the case with Indian strains of malaria. Its prophylactic value is very similar to that of the cinchona alkaloids.

(6) In blackwater fever and in patients in whom administration of quinine produces hæmoglobinuria atebrin can be safely given.

(7) The blood pressure is lowered in some patients during the administration of the drug, but in the majority there is no effect. The pulse rate and respiration are not markedly affected. It has been used in patients suffering from endocarditis and myocarditis without ill-effects.

(8) The drug is largely excreted in the urine and can be readily detected in it. The excretion is not regular, occurs in fits and starts, and goes on for three weeks or longer. There

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A CASE OF TROPICAL TYPHUS SEROLOGICALLY RELATED TO 'SCRUB TYPHUS' OF THE FEDERATED MALAY STATES

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IN a recent publication, Kundu (1932) described a case of typhus fever contracted in Burma, the clinical diagnosis being confirmed by a strongly positive Weil-Felix reaction with proteus X19. In the conclusions to his paper Kundu refers to the possibility of the tropical

(Continued from previous page)

is a distinct tendency towards cumulative action of the drug in the body.

(9) Atebrin produces certain untoward effects which are not however serious. A profound feeling of general depression occurs in some patients. A slight yellow tinge of the skin and conjunctiva was observed particularly in those patients in whom excretion from the kidney is hindered for some reason. Slight epigastric pain, a feeling of uneasiness in the stomach, headache and loss of appetite and diarrhoea sometimes occur when the drug is being administered. These as a rule stop when the drug is stopped.

(10) The action of atebrin closely resembles that of the cinchona alkaloids and the introduction of this drug is a distinct advance in the treatment of malarial fevers in India. The price at present is too high for its use by the people in general.*

REFERENCES

- Green, R. (1932). A Report of Fifty Cases of Malaria treated with Atebrin. *Lancet*, Vol. I, p. 826.
- James, S. P., and others (1932). A Discussion on Synthetic Anti-malarial Remedies and Quinine. *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXVI, p. 105.
- Knowles, R., and Das Gupta, B. M. (1932). Clinical Studies in Malaria by Cultural and Enumerative Methods. *Indian Med. Gaz.*, Vol. LXVII, p. 432.
- Napier, L. E., and Das Gupta, B. M. (1932). Atebrin: A Synthetic Drug for the Treatment of Malaria. *Ibid.*, p. 181.
- Napier, L. E., Butcher, D., and Das Gupta, C. R. (1932). Field Experiments with Atebrin and Plasmo-chin. *Ibid.*, p. 186.
- Schulemann, W. (1932). Synthetic Anti-malarial Preparations. *Proc. Roy. Soc. Med.*, Vol. XXV, Part I, p. 897.

(*The present price of atebrin is Rs. 49-8 for 300 tablets, that is Rs. 2-8 for one 'treatment' of 15 tablets; of this sum 23 per cent, or 9 annas, is duty. It is hoped that the government will shortly see their way to allow this useful drug to be brought free of duty into India, as at present it is into Ceylon.

A single 'treatment' can be purchased, but the price is a few annas more per 'treatment'. On the other hand the makers are prepared to quote a considerably lower rate for quantities of 5,000 tablets or more.—EDITOR, I. M. G.)

typhus which occurs in Malaya overlapping into Burma, and suggested that further investigation in the future would probably reveal the presence in this country of more cases of fever of this type.

Experience in Malaya has shown (Fletcher, 1930) that in that country 'tropical typhus' of two distinct serological varieties is met with. The first of these occurs among the urban population and is designated the 'W' group or 'shop typhus'. The serum of patients suffering from this type of the disease gives a positive agglutination reaction with the ordinary X19 strain of proteus. The other variety, occurring among the rural population, is called the 'K' group or 'scrub typhus' and differs, *inter alia*, from the urban variety in that the serum of the patients does not agglutinate proteus X19 but gives a positive Weil-Felix test with the 'Kingsbury' strain of proteus, proteus XK. To this latter group of typhus-like fevers, according to Fletcher, belongs also tick typhus of India.

Apparently the case described by Kundu corresponds to the 'shop typhus' met with in Malaya.

Cases of 'tick typhus', i.e., typhus-like fevers apparently conveyed by the bite of ticks and probably also of mites, have been reported relatively frequently from India (Megaw and Rao, 1928; Christian, 1932). In such cases the Weil-Felix reaction has been found extremely variable, the majority being negative when proteus X19 is used. The 'Kingsbury' strain, proteus XK, does not appear to have been actually employed in the diagnosis of such cases in India, except in the one case reported by Christian (1932), where the serum of the patient, which gave a negative result in a dilution of 1/25 with the non-motile 'O' variant of proteus X19, weakly agglutinated—perhaps in hardly significant titre—the 'O' variant of proteus XK. It is therefore not certain to what extent, if any, the typhus-like fevers of India fall into two serological groups corresponding to the 'W' and 'K' groups of similar fevers occurring in Malaya.

So far as we are aware, no cases of tick typhus nor cases of typhus-like fevers corresponding to the 'K' group, or 'scrub typhus', of the Federated Malay States, have hitherto been reported from Burma. The following case, which clinically resembled the one and which laboratory investigation showed to be related to the other, may therefore be of interest, not only as showing that such cases may be met with in Burma but as lending support to Kundu's suggestion regarding the possible identity of these fevers here and in Malaya:

HISTORY AND CLINICAL FEATURES OF THE ILLNESS

Mr. G. F. B., an European, aged 40 years, was admitted under the care of one of us (C. de C. M.) in the Rangoon General Hospital on 27th December, 1932. The previous history was that he was touring in the forests of the Thayetmyo district of Upper Burma

when on 18th December he felt feverish and developed severe pains in all his joints accompanied by a severe frontal headache. He had suffered from dengue fever on previous occasions and thought that this was a similar attack.

On 22nd December he returned to headquarters and reported to the civil surgeon, Thayetmyo. His temperature rose gradually to 102°F., while the pulse rate remained round about 70.

On the day after his return to Thayetmyo, a profuse rash appeared all over his body and his general condition became worse, so he was transferred to Rangoon and was admitted to the Rangoon General Hospital on 27th December, 1932, the ninth day of the illness.

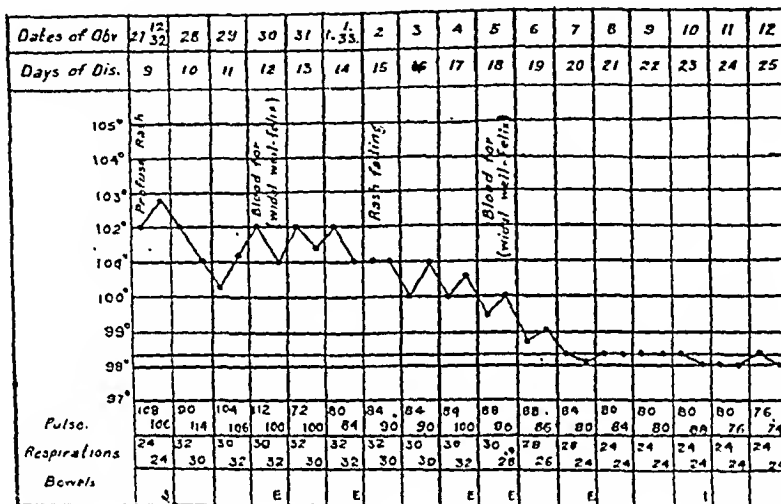
On admission he stated that he had had T.A.B. inoculation in November 1931, had last suffered from dengue in July 1932, and had severe attacks of malaria in 1922 and 1923.

By the 2nd January, the spleen had further enlarged and appeared to be very tender, and the liver could now be felt two fingers' breadth below the costal margin. The left heart was enlarged, and the action so bad that strophanthin, gr. 1/200, was given intravenously with benefit. The rash at this time—about the 15th day of the illness—began to fade and was replaced later by a general hyperæmic condition of the skin, which showed definite staining.

From the 4th January (17th day of the disease) the temperature began to fall by lysis, reaching the normal line on the 7th January. With the defervescence the general condition improved. Consciousness returned and the pulse became more regular.

By the 16th January the liver had become normal, the spleen only just palpable, and the last signs of the staining of the skin had disappeared.

Patient G. F. B. Typhus Fever



No history giving any clue to the possible source of infection in his present illness was obtained from the patient himself, but his wife stated that the day he returned from the jungles, he complained of a painful insect bite on the forearm. He did not know what the biting insect was, nor did he know when he had been bitten.

On examination, his temperature was 102°F., pulse 108 and respirations 24. The whole trunk and limbs were covered with a large and profuse, deeply-pigmented, maculo-squamous rash. There was no rash on the face nor on the palms and soles. The face was flushed, conjunctivæ injected, tongue coated, spleen enlarged four fingers' breadth below the costal margin, liver not palpable. The heart was irregular and showed extra-systoles.

The blood was repeatedly negative for malaria parasites.

From the day of admission until the 3rd January, the temperature ranged between 101°F. and 103°F., the four-hourly chart showing a maximum rise on one occasion to 104.2°F. The pulse throughout seldom rose above 108 and was more often between 80 and 90.

The patient appeared to be acutely ill throughout and soon fell into a low muttering delirium which on occasions became wild and could only be controlled by morphia.

The heart was slow, feeble, and markedly irregular, with dropped beats, and the pulse of low tension.

From now on he made a rapid and uninterrupted convalescence and was discharged from hospital on 25th January, 1933.

The clinical features of the illness, together with the history of an insect bite and the negative character of the serological findings during the patient's stay in hospital, appeared to justify a tentative diagnosis of tick typhus.

Serological investigations

In attempting to arrive at a diagnosis in G. F. B.'s case, which clinically appeared to rest between enteric group infection or some form of typhus fever, the latter being more probable, the patient's serum was examined at intervals during the course of the illness, on three occasions by the Widal test for evidence of enteric fever, and on two occasions by the Weil-Felix test for evidence of typhus fever.

For the Widal tests both Felix's 'qualitative receptor analysis' method (Felix, 1930) and Dreyer's method were used. The Widal tests were complicated by the fact that the patient had received T. A. B. inoculation about a year previously. The results of all the tests are given in tabular form below:

Widal tests for enteric group infection

Specimen taken on	Day of disease	Method used	RESULTS				
			Serum dilution	T 'H' 901	T 'O' 901	Para A 'H' A6	Para B 'H' B2
24-12-32	6th	Felix's	1-25	++H0	++0	±0	+0
			1-50	++H0	+0	—	±0
			1-100	+H	—	—	—
			1-200	±H	—	—	—
			Control	—	—	—	—
30-12-32	12th	Felix's	1-25	++H	++0	++H	+H
			1-50	++H	+0	++H	+H
			1-100	+±H	—	+H	+H
			1-200	+H	—	+H	—
			Control	—	—	—	—
5-1-33	18th	Felix's	1-25	+++H	++0	++H	+++H
			1-50	++H	++0	++H	+++H
			1-100	+H	++0	+H	+++H
			1-200	±H	±0	—	+++H
			Control	—	—	—	—
			Standardized suspension	Dilution giving standard agglutination		Reduced titre 'R. T.'	
30-12-32	12th	Dreyer's	<i>B. typhosus</i> 'H' ..	1-170		21	
			<i>B. para A</i> 'H' ..	1-680		170	
			<i>B. para B</i> 'H' ..	1-50		10	
			<i>B. typhosus</i> 'O' ..	1-15		0.9	
			<i>Bact. artrycke</i> 'O' for Para B 'O'.	Negative		0	
5-1-33	18th	Dreyer's	<i>B. typhosus</i> 'H' ..	1-250		31	
			<i>B. para A</i> 'H' ..	1-500		125	
			<i>B. para B</i> 'H' ..	1-75		16	
			<i>B. typhosus</i> 'O' ..	1-17		1	
			<i>Bact. artrycke</i> 'O' for Para B 'O'.	Negative		0	

Note.—+++ denotes complete agglutination; ++ strong, almost complete; + partial, visible with the naked eye; ± trace of agglutination, visible with lens; — no agglutination. H=floccular agglutination; 0=granular, small-flaking, agglutination.
For interpretation of Dreyer's test see Gardner (1931).

The Weil-Felix tests were carried out with the same technique as that used for Felix's method in the Widal tests, on the 12th and on the 18th day of the disease. Living cultures of proteus OX19, which gives only small-flaking agglutination, were used. The results were entirely negative in dilutions from 1 in 25 to 1 in 200.

Comments.—In assessing the diagnostic value of the Widal tests, the 'H' agglutination given by the patient's serum must be discounted, in view of the comparatively recent inoculation with T. A. B. vaccine. The lack of significance of this agglutination is further supported by the fact that repeated tests showed no marked increase in the titre in respect of any one member of the enteric group.

The only finding which was at all suggestive of enteric infection in these tests was the definite rise in the titre of *B. typhosus* 'O' agglutination, which showed strong positive in 1—100 by Felix's method at the third test with the 18th day specimen. According to Felix (1930) such a reaction is at least highly suggestive of enteric group infection even in an inoculated patient. One of us (L. A. P. A.) has, however, observed titres of this magnitude not uncommonly in the sera of healthy inoculated persons in this country, indeed also occasionally in healthy uninoculated persons, when using the highly sensitive culture T 'O' 901 with Felix's technique. Moreover, the results obtained by Dreyer's technique, using the highly agglutinable Oxford standard suspension of *B. typhosus*

'0', entirely negatived the presence of '0' agglutinins in any significant quantity in the patient's serum.

From these tests, therefore, a negative report was given as regards enteric group infection.

The Weil-Felix test, using proteus OX19, was completely negative; consequently no diagnosis of the case by serological methods could be made at this time with the materials at our disposal.

Some time after the patient had completely recovered and had left the hospital, the Pasteur Institute, Rangoon, received, through the kindness of Dr. P. H. Martin of the Institute for Medical Research, Kuala Lumpur, cultures of the 'Kingsbury' strain of proteus, proteus OXK.

This strain, the history of which is given by Felix and Rhodes (1931), reacts specifically with the serum of patients suffering from that group of 'tropical typhus' which has been referred to above as occurring among the rural population of the Federated Malay States and which is designated group K (= rural group), or more recently 'scrub typhus' (Fletcher, 1930); the serum of patients suffering from this variety of typhus fever invariably fails to react with the usual X19 strain.

Some of the serum of patient G. F. B., drawn on the 18th day of the disease, was still available, having been kept in the refrigerator since its receipt in the Institute. After the proteus OXK cultures received from Kuala Lumpur had been found to conform to the necessary biochemical and serological tests, the serum of the patient was put up against this strain.

The test was carried out by Dreyer's method using living saline suspensions, with 18-24 hours incubation in the water-bath at 37°C. The result was as follows:—

Dilutions of serum	Degree of agglutination with strain OXK	Type of agglutination
1-25	Total	'0'
1-50	Total	'0'
1-125	Total	'0'
1-250	Total	'0'
1-500	Total	'0'
1-1,000	Total minus	'0'
1-2,500	Standard minus	'0'
1-5,000	Negative	..
Control	Negative	..

A further test on the same day, using proteus OX19, was again completely negative in all dilutions from 1-25 upwards.

Comments.—The serum, which repeatedly failed entirely to agglutinate proteus OX19, gave partial agglutination, easily visible with the naked eye, in a dilution of 1-2,500 when tested with the 'Kingsbury' strain, proteus OXK. This titre is comparable to those observed in cases of 'scrub typhus' occurring in

Malay. There appears to be little doubt that this case was, in fact, 'tropical typhus' and belongs to the same group of this disease as the 'scrub typhus' of Malaya.

Summary and conclusions

1. A case of continued fever contracted in Burma and exhibiting symptoms and signs suggestive of 'tropical typhus' is described.

2. Repeated Widal tests carried out at intervals during the course of the illness gave no evidence of enteric group infection, while the Weil-Felix test, using proteus OX19, was persistently negative.

3. The serum of the patient, taken on the 18th day of the illness, strongly agglutinated the 'Kingsbury' strain of proteus, OXK, a strain of proteus which reacts specifically with the serum of cases of 'scrub typhus' occurring in Malaya.

4. It is considered, therefore, that this case was one of tropical typhus belonging to the same serological variety of the typhus-like fevers as the 'K' group, or 'scrub typhus', of the Federated Malay States.

5. The clinical features of the case, with a history of a painful insect bite, and the later serological findings, strongly suggest that we are dealing here with a variety of tick typhus, forming another of the rural group of typhus-like fevers, a group which includes tick typhus of India on the one hand, and scrub typhus of Malaya on the other.

6. So far as we are aware, this is the first occasion on which this variety of tropical typhus has been reported in Burma and demonstrated serologically. We suggest that the introduction and use of the 'Kingsbury' strain of proteus, in addition to proteus X19 for the serological diagnosis of typhus-like fevers in this country, will probably show that, here, as in Malaya, there exist two groups of these fevers, one of which has hitherto remained undiagnosed by laboratory methods.

REFERENCES

- Christian, C. R. (1932). A Case of Typhus due to Tick Bite. *Journ. Roy. Army Med. Corps*, Vol. LIX, p. 445.
- Felix, A. (1930). The Qualitative Serum Diagnosis of Enteric Fevers. *Lancet*, Vol. I, p. 505.
- Felix, A., and Rhodes, M. (1931). Serological Varieties of Typhus Fever. *Journ. Hyg.*, Vol. XXXI, p. 225.
- Fletcher, W. (1930). Typhus-like Fevers of Unknown Aetiology with Special Reference to the Malay States. *Proc. Roy. Soc. Med.*, Vol. XXIII, Part II, p. 1021.
- Gardner, A. D. (1931). Technique of Serological Reactions. *System of Bacteriology in Relation to Medicine*, Vol. IX, p. 184. London: His Majesty's Stationery Office.
- Kundu, M. L. (1932). A Case of Typhus Fever in Rangoon. *Indian Med. Gaz.*, Vol. LXVII, p. 390.
- Megaw, J. W. D., and Rao, S. S. (1928). Tick Typhus and other Sporadic Fevers of the Typhus Group. *Indian Med. Gaz.*, Vol. LXIII, p. 306.

THE ROLE OF THE EOSINOPHILES IN THE DIAGNOSIS OF SPASMODIC ASTHMA

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HISTORICAL

Sputum.—Eosinophiles were first noted in the sputum of asthmatics in 1889 by Von Muller and by Gollasch. In 1892 Aranson and Phillip found that 66 per cent of the cells in the sputum of a patient with asthma were eosinophiles. Weiss (1891), Lewy (1900), Heineke and Deutschmann (1906), and Von Strumpell (1908) found eosinophiles in the sputum in cases other than asthma and considered that the presence of eosinophiles in sputum was not specific for asthma.

Blood.—Fink (1890), Neusser (1892), Mandybur (1892), and Von Noorden (1892) found that at the time of the attacks there was usually an increase in the number of eosinophiles in the blood. Von Noorden reports a case with 33 per cent of eosinophiles during an attack and 5 per cent during a free interval. Gabritschesky (1893) found a well-marked eosinophilia in three cases. Zappert (1893) and Wolff (1900) each reported the finding of about 10 per cent of eosinophiles in the blood of asthmatics during intervals of freedom from attacks. Billings (1897) had a case with 54 per cent of eosinophiles. Herrick (1911) reported a case with a total leucocyte count of 57,000 of which 77 per cent were eosinophiles. Staubli (1911) considered that eosinophilia was a constant sign of asthma.

Variability of the sign.—It will be seen that presence of eosinophiles in the sputum and the blood of asthmatics has long been known. The marked variability of this sign in different cases and at different intervals in the same case requires a passing reference before the causation of eosinophilia and its diagnostic value is discussed. Von Noorden (1892) reports a case with 33 per cent eosinophiles during an attack and only 5 per cent during a free interval. On the other hand Heineke and Deutschmann (1906) observed during an asthmatic attack a decrease in blood eosinophilia from 2.1 to 0.4 per cent. Bray (1931) records a case in which there was an eosinophile count of 18 per cent of a total leucocyte count of 11,600 in the free interval dropping to an entire absence of eosinophiles in a count of 23,700 leucocytes during the attack. Gillespie (1930) found that during the attack the eosinophilia percentage in a majority of cases fell to nearly half of that during the free intervals. Rackemann (1918)

in a clinical study of 150 cases of asthma stated that the percentage of eosinophilic leucocytes in the blood did not vary during and between the attacks, and that increased blood eosinophilia was not a constant sign of asthma. Huber and Koessler (1922) stated that 25 to 30 per cent of all cases of asthma were bacterial in origin and that blood eosinophilia in this group of cases varied exceedingly sometimes being very marked, sometimes slight, and sometimes even completely absent. Brown (1927) stated that eosinophilia in bronchial asthma was by no means a constant finding. Sputum eosinophilia is subject to the same variations. Knott (1930) found that out of 132 cases the sputum was eosinophilic in 85 cases. In our series of 150 cases only 36 had eosinophiles in the sputum.

THE CAUSATION OF EOSINOPHILIA

I. The earliest theory about the causation of eosinophilia is that of Neusser who in 1892 stated that eosinophilia was produced in response to the increased activity of glands supplied by the sympathetic nervous system. His views have never been confirmed. Eppinger, Falta, and their co-workers (1907) on the other hand saw in eosinophilia a symptom of increased vagus tone. This view has some adherents. Hajos and Enyedy (1925) in a study of 30 cases of asthma concluded that eosinophilia was an early indicator of vagus irritability.

Bezançon and Bernard (1930) suggest that eosinophilia may be evidence of the vagotonic state. McDowall (1930) suggests that eosinophilia in cases of asthma may be due to increased secretion of insulin brought about by increased vagus tone. He argues his point on the following lines: (i) that both McLeod and Clark have shown that stimulation of the vagus causes a fall of blood-sugar level, presumably by causing the pancreas to secrete insulin; (ii) that Cameron has shown that asthmatics commonly have a low blood-sugar level; and (iii) that Lawrence has shown that in diabetes the administration of insulin causes eosinophilia.

II. The causation of eosinophilia in asthma has been looked upon from an entirely different point of view since this disease has been associated with the phenomenon of anaphylaxis. In 1905 Stehastnyi showed that blood and serum injections into animals were often followed by a considerable increase in the number of eosinophiles in the blood. In 1910 Moschowitz noted the association of eosinophilia with anaphylaxis. He took the position that anaphylactic disease was invariably associated with eosinophilia, that asthma was also associated with eosinophilia, therefore asthma was the result of anaphylaxis. The true connection between eosinophilia and the anaphylactic process was first clearly recognized by Schlecht in 1910. He observed marked increase in the number of eosinophiles after serum injection and he

ascribed this phenomenon to the introduction of the foreign protein. In 1912 Schlecht and Schwenker found that eosinophilia developed regularly on re-injection of egg albumin, serum albumin or globulin into animals which had been sensitized by a previous injection of a minute dose of the same substance. They discovered also the eosinophilic infiltration of the bronchi in the lungs of anaphylactic guinea-pigs. Since then the consensus of opinion has been in favour of considering eosinophilia as a manifestation of a condition of allergy that has been shown to exist in asthma, hay fever, urticaria, etc. Hiss in 1914 considered that the eosinophile diathesis was the basis of the allergic condition.

On the basis of Schlecht and Schwenker's work eosinophilia was considered as a protective reaction of the organism against certain definite decomposition products of protein origin. In this connection the views of Berger, Alexander, and Meulengracht and Holm require attention. Berger (1916) noted that when a protein which an infant had never previously ingested, was introduced into that infant's diet there was usually an increase in the percentage of eosinophiles in the general circulation. Alexander (1928) has suggested that protein-like substances are broken down through the action of eosinophiles. Meulengracht and Holm (1930) have shown that ingestion of raw liver constantly induces an eosinophilia in individuals suffering from certain diseases, but liver or liver-extract does not do so. Huber and Koessler (1922) are in complete agreement with Schlecht and Schwenker and believe that most clinical eosinophilias have to be considered as the reaction of a person in the state of allergy. In asthma they believe that 'it is evidence of (a) the allergic type of asthma due to sensitization with proteins of antigenic character, or (b) of an intoxication with higher peptones. If constantly absent it forms, together with other clinical symptoms, strong evidence that asthma is due to intoxication with lower peptones or with the amines, or that the bronchospasm is produced by extraneous factors, pressure on the vagus by tumours or aneurism'.

Zambusch (1927) suggested that eosinophilia in allergic conditions was due to defective splenic function, normal action of the spleen being to 'hem in' the eosinophile cells.

III. Coates and Ersner (1930) consider the eosinophilia a factor in all inflammations irritative rather than infective in character and it is a constant component when the tissues are oedematous. Bezançon and Bernard (1930) in their review of the French literature on the subject considered that the eosinophile is a connective tissue cell and is associated with the repair that takes place at the site of injury. Local eosinophilia first occurs at the site of reaction and increase in the eosinophiles of the blood takes place secondarily.

Having considered the different views about eosinophilia we now proceed to give our views on the subject. We will begin by taking into consideration the responses in the blood to the injections of various foreign substances. The antigens injected into the body consist of two classes, (i) those of plant origin and (ii) those of animal origin. The plant proteins injected into the body are generally dead bacilli and tissues react against them by local capillary dilatation followed by migration of the polymorphonuclear leucocytes. The dead bacilli are taken up by these neutrophils and destroyed, and at the same time substances are produced which lyse and break up the dead bacteria into soluble non-toxic bodies. Following the injections of dead bacilli the animal shows a temporary increase in the number of polymorphonuclear cells in the blood, at the same time various immune substances, agglutinins, lysins, and bactericidal substances can be demonstrated. We can therefore inject plant proteins into an animal body and get a series of responses called immunity. On the other hand when we inject foreign animal proteins into an animal the response is differently expressed depending on whether the substance injected is a mass, like cells, or in a soluble state. When particles like cells are injected there is a local response containing many eosinophile cells and the foreign cells themselves are broken up and destroyed. In time there is a general increase in the eosinophiles of the blood and lytic substances are found, such as haemolysins. When soluble particles or particles in the colloidal state are injected the eosinophiles increase in the blood and various substances such as precipitins form to deal with the foreign protein. When large doses are injected such as antidi-phtheritic serum, an increase in the eosinophiles is observed followed by toxic phenomena which are known as serum sickness.

Hitherto we have been dealing with large particles or particles in the colloidal state, we can now consider the injection of crystalloidal substances derived from these plant and animal proteins. The best known examples are histamine and tyramine which are obtained from the amino-acids of plants and animals. The injection of both these substances causes a temporary increase in the eosinophiles of the blood, while on the other hand pilocarpine which is a plant alkaloid also gives rise to an eosinophile response. Most of the plant alkaloids, such as morphine, quinine, and strychnine, do not cause an increase in the percentage of eosinophiles in the blood. We therefore see that eosinophilia is a response to the injection of foreign animal protein as well as of certain amines which can be derived from the amino-acids of plants or animals. On the other hand increase in polymorphonuclear cells is a response of the body to deal with particles of plant proteins. Most of the plant alkaloids do not cause a response of either type of cell.

The next point to be considered is the difference in the reactivity of different individuals. To illustrate this point we may here quote a small series of experiments (table I). Repeated injections of peptone, aolan, and egg albumin were given to six patients, two getting peptone injections, two aolan, and the remaining two egg albumin. On comparing the blood counts in case 1 with 2, case 3 with 4, and case 5 with 6 it will be evident how different individuals react differently to the same substance. In case 1 peptone injections did not cause any appreciable rise in the eosinophile count, while the same substance gave rise to a marked eosinophilia in case 2. The same thing can be seen in cases of egg albumin and aolan.

the attacks subsided. Signy and Bray (Bray, 1931) in 100 cases of children found the eosinophile percentage varying from 4 to 7, the highest being 23.

Spangler (1925) considers the eosinophilic index an important guide in determining the degree of hypersensitivity of a patient, but Baagoe (1928) finds that there may be a marked sudden rise in the eosinophilic counts of asthmatics without any associated symptoms and on the other hand that repeated severe paroxysms may occur in other patients with little or no rise in eosinophilia. Van Leeuwen and Van Nickrek (1928), after a study of 203 patients, also discredit the value of eosinophilia as an index of the severity of the condition and the

TABLE I

Experiment number	Substance injected	Blood count before injection	BLOOD COUNT AFTER			
			first injection	second injection	third injection	fourth injection
1	Peptone	Total leucocytes 10,000	10,200	12,000	9,000	..
		Total eosinophiles 1,000	918	2,400	1,260	..
2	Peptone	Total leucocytes 26,000	26,000	15,000	15,000	..
		Total eosinophiles 0	2,080	7,000	5,000	..
3	Aolan	Total leucocytes 12,000	7,000	10,000	10,000	7,000
		Total eosinophiles 600	600	800	2,000	1,000
4	Aolan	Total leucocytes 20,000	18,000	20,000	12,000	28,000
		Total eosinophiles 2,000	1,800	2,000	6,000	14,000
5	Egg albumin ..	Total leucocytes 12,000	14,000	15,000	11,000	..
		Total eosinophiles 800	1,000	2,000	1,100	..
6	Egg albumin ..	Total leucocytes 15,000	20,000	25,000	25,000	..
		Total eosinophiles 600	2,000	12,500	16,000	..

The value of the eosinophile count.—Cooke (1921) reports eosinophiles in excess of 4 per cent in 63 per cent of a series of 90 carefully-studied cases. According to him blood eosinophilia is therefore suggestive evidence of bronchial asthma, but its absence does not preclude such a diagnosis. Spangler (1925) considers that increased eosinophilia in bronchial asthma points to the presence of an allergic factor in the disease. Brown (1927) in 193 cases of asthma found the average eosinophile count, both in sensitive and non-sensitive cases, to be 7 per cent—this is higher than the average obtained in cases suffering from hay fever (6 per cent), colds (3 per cent), eczema (5 per cent), and urticaria (4 per cent). Rackemann and Colmes (1929) found more than 4 per cent of eosinophiles in the blood of practically all of 150 patients with asthma. Baagoe (1928) in the study of eosinophiles of normal children found that the percentage varies from 0 to 12 with an average of 3 per cent and slowly falls as the child gets older. In asthmatic children an increase occurred in the eosinophiles after

progress of the patient. Brown (1927) found that some definitely sensitive patients had no eosinophilia either during or between attacks, whilst some of the highest percentages were in non-sensitive or bacterial cases. He concludes that sex, age, and sensitivity play no part in determining the degree of eosinophilia. In our series of cases also some of the highest eosinophile counts were encountered in the bacterial cases.

So that it will be seen that there is a good deal of confusion regarding the value of this sign in asthma. We will now proceed to discuss this point.

The material we studied consisted of 150 individuals who were suffering from typical spasmodic asthma. Many of our patients had also various infections common in the tropics, which made the problem still more difficult as the leucocyte count varied from 5,000 to 37,000 per cubic millimetre. Under such conditions it was obviously impossible to use percentages; these would be meaningless unless one did the total count as well. This has been done

throughout and the eosinophiles given as a number per cubic millimetre and not as a percentage. At the same time it is necessary to define what we mean by a normal count and to give the limits of leucopenia and leucocytosis. In Bengal there are two common diseases that produce leucopenia, namely kala-azar and chronic malaria with splenomegaly. Leucopenia is marked in kala-azar, we have therefore chosen this disease to establish what we mean by leucopenia. Table II shows the counts of 101 individuals who were suffering from kala-azar in which parasites were found either by spleen puncture or blood culture. Many of these cases were also suffering from hookworm infection.

and were admitted into the Medical College Hospital. These cases were either of primary pneumonia or of pneumonia secondary to debilitating diseases like malaria, kala-azar, and hookworm. The leucocyte count varies from 5,000 per cubic millimetre to 50,000. Taking 8,000 leucocytes as the lowest normal count there were 11 cases that showed leucopenia, the majority of these must have been secondary to diseases like kala-azar. The next point to decide was, what should be the upper limit of a normal count, because it is well known that these cells vary in number according to the meals taken during the day and to other causes. We have selected 12,000 as the upper limit of a normal count. In these cases there were 72

TABLE II
Kala-azar—many complicated with hookworm

Leucocytes under	Eosinophiles under											TOTAL.
	0	50	100	150	200	250	300	350	400	450	500	
1,500 ..	1	1	2
2,000 ..	2	4	2	8
2,500 ..	11	5	4	..	1	21
3,000 ..	3	..	2	2	1	8
3,500 ..	9	2	2	13
4,000 ..	4	..	2	1	..	2	9
4,500 ..	4	1	1	1	2	1	1	11
5,000 ..	5	3	1	2	2	..	1	1	15
5,500 ..	1	1
6,000 ..	3	..	1	1	..	1	1	7
6,500 ..	1	1
7,000	2	2
7,500	1	2	3
	44	16	18	7	6	4	4	1	1	101

Out of 101 cases only 8 cases show an eosinophilia of over 5 per cent.

We are indebted to Dr. L. E. Napier and the late Dr. J. B. McVail for the use of their research material to compile this table. You will see that the lowest count is 1,500 leucocytes per cubic centimetre and the highest count was 7,500. Taking a 5 per cent basis of the eosinophile count which is shown by the 'step line' it will be seen that in only 8 cases was there over 5 per cent of eosinophilia, in spite of the fact that the majority of these patients had hookworm infection as well. McVail (1922) pointed out that in hookworm infections, if leucopenia is present, the eosinophiles are of little practical use in the diagnosis of this helminthic infection. We may therefore put a limit of leucopenia to a count below 8,000 leucocytes per cubic millimetre.

We will now consider what we will take as the upper limit of a normal count, for this purpose we have chosen pneumonia as a disease illustrating the phenomenon of leucocytosis. Table III shows the leucocyte count of 123 individuals who were suffering from pneumonia

individuals who showed a leucocytosis varying from 13,000 to 50,000 per cubic millimetre. In this series there were only 18 individuals who showed an eosinophilia above 5 per cent. The step line shows the number of eosinophiles per cubic millimetre of blood that constitutes the 5 per cent limit. We will therefore establish as a normal count the variations between 8,000 and 12,000 leucocytes per cubic millimetre, considering any number below that as a leucopenia and above it as a leucocytosis. With leucopenia the number of eosinophiles per cubic millimetre is not a reliable indication of hookworm infection.

We will now study the effect of helminthic infections on the number of eosinophiles per cubic millimetre of blood. Table IV consists of 100 individuals who were suffering from hookworm infection; eggs were found in the stools.

We are indebted to Dr. P. A. Maplestone for supplying us the data for our tables. We will see that for these individuals the count varies

TABLE III
Pneumonia—primary and secondary

Leucocytes under		Eosinophiles under								TOTAL.
		0	250	500	750	1,000	1,250	1,500		
5,000	..	1	3	11 Leucopenia.	4
6,000	2	1		3
7,000	..	1	3		4
8,000	..	3	2	3	40 Normal.	8
9,000	..	1	3	1		5
10,000	..	5	5	2	1		13
11,000	..	2	5	1		8
12,000	..	4	1	..	1		6
13,000	..	2	3	3	1	..	1	..	72 Leucocytosis.	10
14,000	..	1	1	1		3
15,000	..	3	1	1		5
16,000	..	4	1	4		9
17,000	..	1	..	2	1		4
18,000	..	2	1	..	1	..	1	..		5
19,000	..	4	1	3	..	1	1	..		10
20,000	..	1		1
21,000	..	3	1	..		4
22,000	..	1	..	2		3
23,000	1		1
24,000	..	1		1
25,000	..	1	..	2	1		4
26,000	1		1
29,000	..	1		1
30,000	..	3		3
32,000	1	..		1
33,000	..	1		1
35,000	..	3		3
38,000	..	1		1
50,000	..	1		1
		51	32	27	5	2	5	1		123

Out of 123 cases 18 cases show an eosinophilia above 5 per cent.

TABLE IV
Hookworm

Leucocytes under	Eosinophiles under													TOTAL.
	250	500	750	1,000	1,250	1,500	1,750	2,000	2,250	2,500	2,750	3,000	3,250	
3,000 ..	2	1	3
4,000	3	2	5
5,000 ..	4	2	3	..	2	1	12
6,000 ..	4	2	1	..	1	1	9
7,000 ..	3	3	4	2	1	1	14
8,000 ..	3	..	3	..	4	4	14
9,000	1	..	2	1	..	2	3	1	1	..	1	..	12
10,000 ..	2	..	2	4	1	..	1	..	10
11,000 ..	1	..	1	1	..	2	1	6
12,000	1	3	..	1	1	1	7
13,000	1	..	1	..	1	..	3
14,000	1	1	1	3
15,000	1	1
17,000	1	1
	19	14	16	6	12	12	3	6	3	3	1	4	1	100

In 28 cases the eosinophiles are below 5 per cent.

from 3,000 to 17,000 leucocytes per cubic millimetre and that in this series 72 out of 100 showed an eosinophile increase above 5 per cent. Of the remaining 28 individuals who did not show this increase in eosinophiles, 18 showed a leucopenia; this evidence of depression of the bone-marrow function accounts for the reduction in the eosinophile count.

The high blood eosinophilia in cases of filariasis with microfilaria present in the blood contrasts markedly with the absence of this sign in cases with no microfilaria in the blood. Dr. Sundar Rao has kindly supplied us with the total and differential leucocyte counts of 200 cases of filariasis. Amongst the cases with microfilaria present in the blood 62 out of 100 show an eosinophile count over 5 per cent, while only 20 out of 100 cases with no microfilaria show this increase. (The tables showing these counts will be found on page 308 in the June number of the *Gazette*.)

organism produce histamine when cultivated in broth. The local production of the histamine in the bronchi would act directly on the unstriped bronchial muscles and dilate the vessels in the mucosa increasing their permeability. The absorption of histamine would produce a localized eosinophilia and later an increase in the eosinophiles of the blood. Table V shows the analysis of 27 individuals in whom we were able to cultivate these Gram-negative bacilli. Out of the 27 individuals 26 showed an eosinophilia over 5 per cent. The one that did not show eosinophilia had also a leucopenia. We can therefore say when Gram-negative bacilli are found in the sputum we would expect an increase of blood eosinophilia above 5 per cent. The second group of cases are those which we attributed to animal proteins where the product acts on the involuntary muscles of the bronchi and also produces vaso-dilatation of the smaller vessels. These cases are generally considered

TABLE V
Gram-negative bacilli cases

Leucocytes under	Eosinophiles under																		Total.
	250	500	750	1,000	1,500	2,000	3,000	4,000	5,000	6,000	7,000	8,000	9,000	10,000	11,000	13,000	16,000		
6,000	1	1	
7,000	1	2	1	4	
8,000	1	1	1	3	
9,000	2	1	..	1	2	
10,000	2	
11,000	1	1	
12,000	1	1	
14,000	1	1	
15,000	1	1	2	
16,000	1	1	1	..	2	1	6	
17,000	1	1	
25,000	1	1	2	
26,000	1	1	
	..	1	2	6	1	2	1	2	1	2	3	1	..	2	1	1	1	27	

Out of 27 cases 26 cases show eosinophilia.

We are now in a position to investigate the value of the eosinophile count in the diagnosis of spasmodic asthma.

Amongst the 150 cases investigated there were only 49 which showed an eosinophile count of less than 5 per cent. The total count varied from 5,000 to 37,000 and out of these 24 individuals showed leucopenia. The majority of these asthmatics showed an eosinophile count over 5 per cent and we had to analyse these cases further. The cases were divided into three groups; group I consisted of 27 individuals in whom we found a Gram-negative bacillus. This organism was first described by Eyre as occurring commonly in cases of asthma. Knott and Oriel showed that certain strains of this

under allergy. Table VI shows the analysis of 44 of these cases giving the total leucocyte count in relation to the number of eosinophiles. Thirty-six out of the 44 individuals showed an increase of over 5 per cent of eosinophiles. In the tropics the function of the liver and the intestinal tract is of great importance. Fourteen out of these patients showed helminthic infection and 10 of these were cured of their asthma by treating them for their helminthic infection. There were in addition 10 cases in which some dysentery organisms were found; thus in three *Entamæba histolytica* was found, and in seven *Bacillus pseudo-carolinus*, *B. morgani*, or *B. meta-dysenterica*. These patients were treated and cured by emetine or

by vaccine treatment. Thus in the tropics the true allergic cases as seen amongst Europeans are rarely observed by us. The third group of

cases. The total count varies from 5,000 to 37,000 and 36 individuals showed an eosinophile count over 5 per cent. Amongst those who did

TABLE VI
Allergic cases

Leucocytes under	Eosinophiles under																			TOTAL.
	250	500	750	1,000	1,500	2,000	3,000	4,000	5,000	6,000	7,000	8,000	9,000	11,000	12,000	15,000	16,000	18,000	25,000	
5,000	1	1	1
6,000	..	1	1	2
7,000	..	1	1
8,000	..	1	1	..	1	2	5
9,000	..	2	..	1	..	1	1	..	1	6
10,000	..	1	1	1	1	1	1	6
11,000	1	1	2
12,000	1	1	1	1	3
14,000	..	1	2	1	1	5
15,000	1	..	1	1	3
16,000	1	1
17,000	1	1
18,000	1	1	2
20,000	1	1	2
23,000	1	1
25,000	1	1
30,000	1	..	1
37,000	1	1
	4	3	3	5	2	7	3	2	3	1	2	2	1	1	1	1	1	1	..	44

Out of 44 cases 36 cases show eosinophilia above 5 per cent.

TABLE VII
Bronchial cases

Leucocytes under	Eosinophiles under															TOTAL.
	250	500	750	1,000	1,500	2,000	3,000	4,000	5,000	6,000	7,000	8,000	9,000	10,000	12,000	34,000
5,000	..	1	1	1	3
6,000	..	1	..	2	1	4
7,000	..	1	4	2	1	8
8,000	..	2	3	1	..	1	..	1	8
9,000	..	2	3	..	2	1	7
10,000	..	2	2	2	2	1	..	1	10
11,000	..	1	2	1	4
12,000	..	5	2	4	3	1	..	1	16
13,000	..	1	1	1	2
14,000	1	1	2
15,000	..	1	..	1	3
16,000	..	1	2	1	1	5
17,000	1	1	..	2
20,000	1	1	1
23,000	..	2	3
37,000	1	1
	20	17	13	14	1	1	1	2	1	4	..	1	2	..	1	79

43 out of 79 cases show eosinophiles under 5 per cent.

cases were diagnosed as being secondary to disease or infection of the respiratory tract. Table VII shows an analysis of 79 of these

not show an increase of eosinophiles were four cases of tuberculosis and two cases of bronchiectasis, and there were four patients who

were relieved by being treated for their nasal condition. The majority of the cases in this group showing increased eosinophilia were sensitive to dust.

SPUTUM EOSINOPHILIA

Source of the eosinophile cells in the sputum.

—It is now generally accepted that the eosinophiles in the bronchial wall and the exudate have emigrated from the blood. Bezançon and Bernard (1930) still believe that local eosinophilia is the primary factor and the blood eosinophilia a secondary or associated condition. Heineke and Deutschmann (1906) and Huber and Koessler (1922) think that the deposit of eosinophiles in the lungs during a paroxysm is the cause of their diminution in the circulation during an asthmatic attack.

Value of sputum eosinophilia.—Although eosinophiles may be found in the sputum in diseases other than asthma, Huber and Koessler (*loc. cit.*) believe that the coincidence of sputum and blood eosinophilia in the same individual are a pathognomonic symptom of the asthmatic state. Klewitz (1928) states that although blood eosinophilia may not be noted in every case of asthma, he has never found it absent in the sputum. According to him it occurs both in sensitive and non-sensitive cases. Knott (1930) found that out of 132 cases the sputum was eosinophilic in 85 cases. In our series of 150 cases only 36 had eosinophiles in the sputum. Brown (1927) found that the number of eosinophiles in the sputum of patients ran directly parallel with the percentage of eosinophiles in the blood. Knott (1930) also came to the same conclusion, but we have not been able to confirm this point. Steinberg and Figley (1928) found that but few eosinophiles occurred in the cellular exudate, within the lumen, and in the bronchial wall in bacterial asthma. While in allergic asthma numerous eosinophiles occurred in the cellular exudate, in the lumen and the bronchial wall.

CONCLUSIONS

(1) The percentage of the eosinophiles in the blood is of little value unless the total count is also stated and the eosinophiles are best expressed in the number present rather than in percentages.

(2) If leucopenia is present the number of eosinophiles per cubic millimetre of blood is of little practical use for diagnostic purposes.

(3) An increase of over 5 per cent of the eosinophiles in the blood is an important indication of the presence of some foreign animal protein, or of certain amines which can be derived from the amino-acids of plants or animals, and of the patient being sensitive.

(4) In asthma there are three types of case associated with increased eosinophilia—

(a) Cases where the proteins or amines are derived from the gut or from animal emanations.

(b) Bronchial cases with Gram-negative bacilli in the sputum.

(c) Bronchial cases where there is local sensitiveness of the mucosa to dust, etc.

(5) The presence of eosinophiles in the sputum is not a constant finding in asthma.

REFERENCES

- Bray, G. W. (1931). *Recent Advances in Allergy*, London: J. & A. Churchill.
 Brown, G. T. (1927). *Journ. Lab. and Clin. Med.*, Vol. XII, p. 1145.
 Gillespie, M. (1930). *Brit. Med. Journ.*, Vol. I, p. 1139.
 Herrick, W. W. (1911). *Journ. Amer. Med. Assoc.*, Vol. LVII, p. 1836.
 Huber, H. L., and Koessler, K. K. (1922). *Arch. Int. Med.*, Vol. XXX, p. 689.
 Knott, F. A., Oriel, G. H., and Witts, L. J. (1930). *Guy's Hospital Reports*, Vol. LXXX.
 McDowall, R. J. S. (1930). *Practitioner*, Vol. CXXIV, p. 212.
 McVail, J. B. (1922). *Indian Med. Gaz.*, Vol. LVII, p. 366.
 Rackemann, F. M. (1918). *Arch. Inter. Med.*, Vol. XXII, p. 517.
 Spangler, R. H. (1925). *Ibid.*, Vol. XXXVI, p. 779.
 Steinberg, B., and Figley, K. D. (1928). *Journ. Lab. and Clin. Med.*, Vol. XIII, p. 921.

The remaining references have been taken from Bray (1931) and the two following books:—

- Brown, O. H. (1917). *Asthma*. London: Henry Kimpton.
 Coca, A. F., Walzer, M., and Thommen, A. A. (1931). *Asthma and Hay Fever*. London: Baillière, Tindall and Cox.

DIABETES IN CHILDREN

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Introduction.—The diabetic child is of more than usual interest to those working on this disease, not only because it provides them with pure diabetic lesions unaccompanied and uncomplicated by any degenerative changes due to age, but also because it gives them a better opportunity of following up the effects of treatment. The prognosis in cases of diabetes in children was always thought to be a matter of considerable seriousness in the past, but it is not reasonable to take such a pessimistic view at the present day. There is no doubt that, since the advent of insulin, the outlook in these cases has been much brighter; a great deal may be done to improve the condition of the child which, if it does not prolong his life, will certainly make it more comfortable. This is possible because in a child the regenerative powers are at their highest, and hence under proper care and suitable treatment there is a much greater opportunity for the regeneration of the islet cells of the pancreas. The literature on the subject is replete with evidence that there is a much quicker regeneration of the islands of Langerhans in children than in adults. Boyd (1925) has reported an interesting case



A. Before treatment.



Fig. 1.

B. After 10 weeks of treatment.



A. Before treatment.



Fig. 2.

B. After 13 weeks of treatment.

of diabetes in a boy who recovered but subsequently met with an accidental death. At autopsy, the pancreas was found to be normal with the exception of scattered pyknotic nuclei in some of the island cells. Boyd had observed the presence of a very large number of island areas at the periphery of the pancreas, sometimes twelve or fourteen, in a low-power field. Bensley, in commenting on Boyd's paper, said that these small bulbous islands adjacent to a duct resembled those produced in experimental animals by the regeneration of newly-produced islands.

It may be stated with a certain amount of definiteness that, taken properly in hand, the diabetic child should make considerable improvement within a comparatively short time. Such improvement in the general health and in the proper growth and development of the child takes place quickly if the case is properly managed from the beginning. The improvement is sometimes so marked that the child becomes scarcely recognizable within six weeks from the commencement of the treatment. On the previous page are photographs of two of the author's cases which add support to this statement.

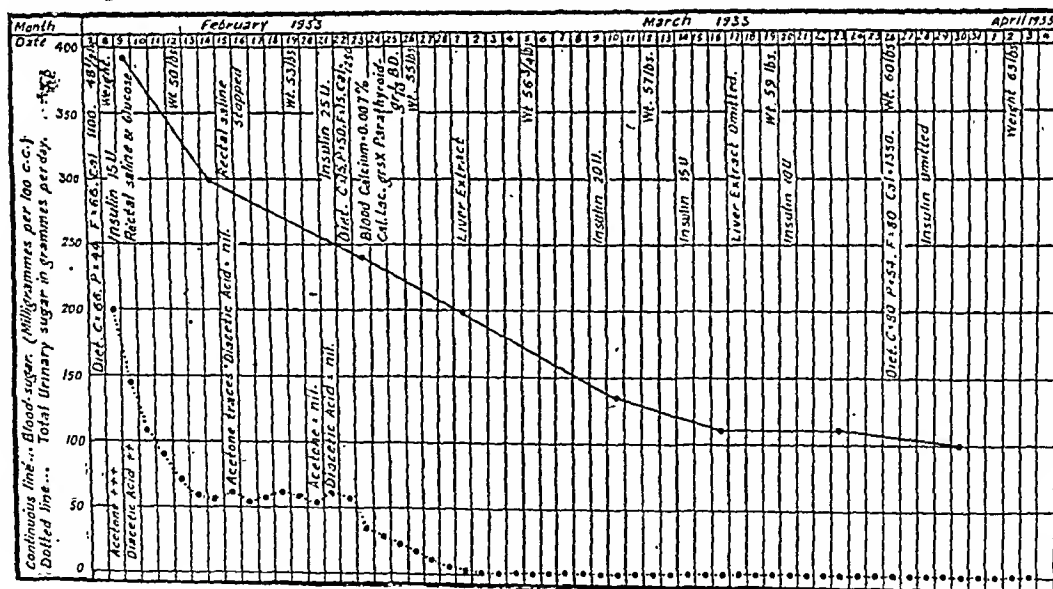
than amongst adults, especially in this country, it is not so very rare as it is usually thought to be. The author had the somewhat unusual experience of having to treat six diabetic children within a space of three months.

Age of onset.—The youngest diabetic child amongst the author's series of cases was a boy aged 1 year and 4 months. The author's experience has been that diabetes is less common in children under 5 years of age. The youngest diabetic child in Joslin's series of cases was a baby 8 months old. Ashby (1923) described the case of a four-months-old diabetic baby with gangrene of the toes. Major and Curran (1925) reported a case with diabetic cataract in a baby 11 months old.

Ætiology.—This is still very obscure. According to many observers, heredity is an important factor. Amongst most of the author's cases, however, heredity could not be traced as playing any important part in the ætiology of the disease. It should be noted here that, unlike diabetes in adults, obesity does not seem to be of any importance as an ætiological factor in diabetes of children. The author is inclined to the opinion that some inherent defect in the endocrine balance of the child, leading to a

Progress of Case (Figure 2). Diabetes Case Sheet.

Name....P.B.H.S. Sex....F. Age....12. Religion....Christian. Physician....Dr. Bose.

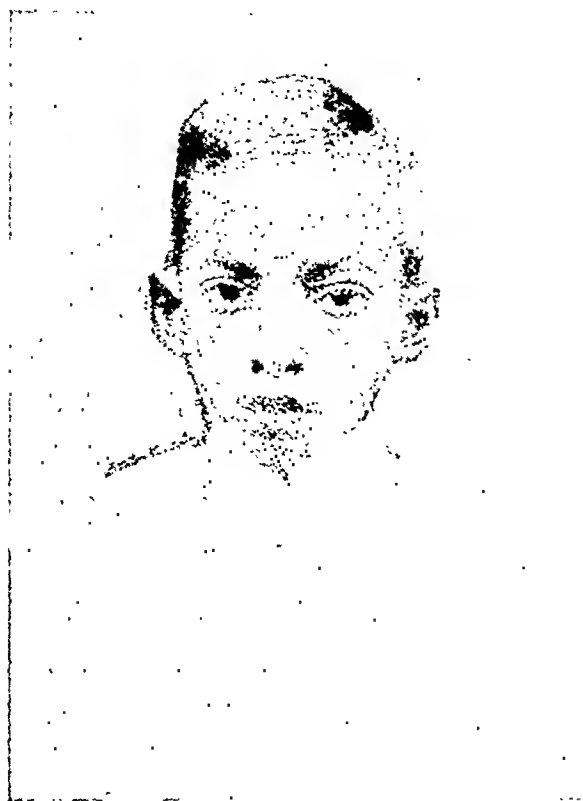


While, therefore, the final prognosis in cases of diabetes in children may not be predicted with any amount of certainty, one should not take too gloomy a view of the disease in the present day of insulin treatment. We know that it is possible now to turn a diabetic child from a living skeleton into a robust healthy being, but whether or not this condition can be maintained permanently, only further research can show.

Incidence.—Though there is no doubt that diabetes is much less common amongst children

disturbance in its normal mechanism, is the causative factor in children, though the exact nature of this disturbance is still obscure.

Onset.—In some of the author's cases the onset was sudden and the course was rapid. Two of the cases were diagnosed for the first time when the patient was in a pre-comatose condition—the child having suddenly become ill with an eruptive fever three days previously. In other cases, the onset was slow and insidious, diabetes being wholly unsuspected in the beginning. The usual history in most of these



A. Before treatment.



Fig. 1.

B. After 10 weeks of treatment.



A. Before treatment.



Fig. 2.

B. After 13 weeks of treatment.

is usually taller than other children of the same age.

The following note, as to the special peculiarities of the diabetic children in her charge, was prepared for the author by an observant staff nurse in charge of the children's ward.

(1) Children suffering from diabetes are more intelligent than other children of the same age.

(2) They are very precocious and quick at understanding.

(3) They are inclined to be very cunning and sly in their ways.

(4) Their nature is very sensitive, and great kindness and tact is required in dealing with them.

(5) At times they are depressed, irritable and

rich in fat; at the same time, it should be remembered that the fat content in the diet should not be too low because fat serves as an important carrier of the fat-soluble vitamin A, which is essential to growth. The following table gives the approximate carbohydrate, fat, protein and the caloric requirement of diabetic children in the different periods of their lives. It should, however, be borne in mind that the proportions given below are only average and have to be varied at times according to the nature of the case and according to complications arising or present:—

Age of the child	REQUIREMENTS PER KILOGRAMME OF BODY-WEIGHT			
	Fat	Carbohydrate	Protein	Calories
1-2 years	3 gms.	12 gms.	4 gms.	90
3-5 "	3 "	9 "	4 "	80
6-8 "	3 "	6 "	3 "	60
9-12 "	3 "	3 "	2 "	50
13-16 "	3 "	2 "	2 "	40

hysterical, and need a little firm handling which usually brings them round quickly.

Treatment.—Though the principle underlying the treatment of diabetic children is more or less the same as that of an adult, yet there is a considerable difference in many essential details. For instance, it should always be borne in mind that the food requirements of growing children are proportionately much greater than those of the adult, and a diet which is insufficient in its total caloric value or inadequate as regards the protein ration may cause serious harm. The growing child requires a generous diet which should not only yield the total caloric value needed according to the age of the child but should contain the proper amount of protein to maintain health and vigor, and to promote growth. It should also be borne in mind that children, as a rule, cannot take the same proportion of fat per kilogramme of body-weight as an adult, and they are more liable to develop acidosis.

The essential difference between the dietetic treatment of diabetic children and adults lies in the fact that, whereas in the case of adults the protein requirement under basal conditions is approximately about $\frac{1}{4}$ gramme per kilogramme of body-weight, in the case of diabetic children the protein requirement varies inversely according to the age—i.e., the younger the child, the greater is the protein requirement per kilogramme. The same rule holds good in the case of the carbohydrate requirement, as well as the total caloric requirement. The fat requirement by diabetic children is also essentially different from that by an adult. The ratio of fat to carbohydrate in the diet of the former should be much less than in that of the latter, because diabetic children are more liable to develop ketosis on a diet disproportionately

rich in fat; at the same time, it should be remembered that the fat content in the diet should not be too low because fat serves as an important carrier of the fat-soluble vitamin A, which is essential to growth. The following table gives the approximate carbohydrate, fat, protein and the caloric requirement of diabetic children in the different periods of their lives. It should, however, be borne in mind that the proportions given below are only average and have to be varied at times according to the nature of the case and according to complications arising or present:—

It will be seen from the above table that the caloric requirement per kilogramme of body-weight, as well as the protein and the carbohydrate requirements, increase inversely according to the age—i.e., the younger the child, the greater is the food and the caloric requirement per kilogramme of the body-weight. The fat requirement, however, has been kept at an arbitrary figure, viz, 3 grammes per kilogramme, but the ratio between the fat and carbohydrate in the diet has been altered by proportionately increasing the carbohydrate quota of the diet. For instance, it will be seen that the proportion of fat to carbohydrate in the first two years of life has been kept as low as 1 to 4, instead of the usual proportion, 2.5 to 1, in an adult diet. As the age increases, the proportion of fat has also been increased in relation to the carbohydrates, so that, at the end of the table, a child between the ages of 13 to 16 years gets a proportion of 1.5 to 1, which somewhat approaches the normal adult proportion.

It should also be remembered by the doctor prescribing diets for diabetic children that he must take into consideration the suitability of the food-stuffs according to the age of the child. For instance, the diets of infants under 2 years should mainly consist of milk. For bigger children, eggs, fish, potatoes, bread, butter, vegetables (those without much roughage), etc., should be prescribed.

Insulin therapy.—The principle of the treatment is the same in children as in adults. If the case is an uncomplicated one and of mild nature, and if the blood sugar is not excessively high, the effect of dieting alone should be tried for a few days, in order to see whether this alone has any effect in reducing the blood and urinary sugar, and in improving the general

health of the child. If dietetic treatment, continued for about a week, fails to make much impression, or if the child loses weight, insulin should be commenced. Of course, if the case is of a severe nature, or if there are complications, insulin treatment should be started at once.

Regarding the dosage of insulin, no hard and fast rules can be laid down, but in as much as the dose may vary in individual cases it should be mentioned here that in children the *proportionate* dose of insulin per kilogramme of body-weight is usually higher than in adults, because of the high carbohydrate content of their diet. It should also be remembered that some of the diabetic children require relatively big doses to make their urine sugar-free. One of the author's cases, a child aged 5 years and weighing only 33½ pounds (or approximately 15 kilogrammes), required as much as 30 units of insulin (given in two doses daily) to make his urine sugar-free.

As a general routine, however, it can be laid down that in mild cases, uncontrolled by diet alone, it is best to commence with small doses of, say, 2 to 3 units once or twice daily. In more severe cases with high blood sugar, commence with 5 to 6 units twice daily. As in the case of adults the dose should be increased gradually until the glycosuria disappears and the blood sugar becomes normal.

It must be remembered that in treating cases of diabetes in children, not only must the urine be kept sugar-free and the blood sugar kept within normal limits, but very careful attention must be given to the proper growth and development of the child. The child must grow in height and gain in weight like other normal children. In cases where the urine is made sugar-free but the child does not grow or gain in weight, the diet must be raised and extra doses of insulin given to keep the urine sugar-free; on the other hand, if the gain in weight is abnormally rapid the diet should be cut down and the dose of insulin adjusted accordingly.

To save space, the author has not included any case records in the present paper; those readers, who are interested in the practical details of treatment in such cases, are however referred to a previous paper published by the author (1930).

Prognosis.—It is undoubted that insulin has made a huge difference in the prognosis. It has not only helped to make their lives comfortable, but it has prolonged the lives of these children and made it possible for them to grow and develop almost normally. Joslin's statement with regard to this point is very apposite, he says 'Thirty years ago, when I began treating diabetic children, I counted the days they lived. It is hard to believe, but it is true, that I am now beginning to measure their lives in decades'.

(Continued at foot of next column)

A SCHEMATIC REPRESENTATION OF THE VARIANTS OF CHOLERA VIBRIO PRODUCED UNDER THE INFLUENCE OF BACTERIOPHAGE

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IN endemic centres of cholera such as Calcutta and in areas where cholera occurs in epidemic form, vibrios can be isolated not only from cholera cases but also from contacts, healthy individuals, waters, flies and other sources. These vibrios may be divided into two great classes, vibrios that are agglutinable by a specific cholera serum and those that are not agglutinable by this serum. The characters of these two classes of vibrios are given below:—

Class I. *Vibrios agglutinable by cholera serum.*

A. *The vibrio of endemic and epidemic cholera.*—The definitely agglutinating vibrio obtained from undoubted clinical cases of cholera during an epidemic of the disease is universally recognized as the true cholera vibrio. The Japanese authors (Inouye and Kakihara, 1925) have recognized three serological types designated by them as 'V. cholera 1, 11 and 111'. We have evidence, which we shall present in a later publication, that there is more than one serological type of cholera vibrio amongst the agglutinating vibrio isolated by us from clinical cholera cases.

B. *The 'El Tor' vibrio.*—These vibrios were isolated at El Tor from the intestines of pilgrims who had died with dysenteric symptoms and who had shown no clinical symptoms of cholera. There were no cases of cholera in the vicinity. The El Tor vibrios give the serum reactions of true cholera vibrio, but differ from the latter in having marked hæmolytic action. There is considerable difference of opinion as to whether these vibrios are to be regarded as belonging to a distinct species or as true cholera vibrios. Recent investigations have shown that cholera vibrios may develop, lose, or show wide variations in their ability to produce hæmolysins. We have studied the hæmolytic properties of nearly 300 freshly-isolated strains of cholera vibrios and have confirmed these observations. The property of causing lysis of red blood cells

(Continued from previous column)

REFERENCES

- Ashby, H. T. (1923). *Lancet*, Vol. I, p. 22.
Bose, J. P. (1930). *Indian Med. Gaz.*, Vol. LXV, p. 197.
Boyd, G. L., and Robinson, W. L. (1925). *Amer. Journ. Path.*, Vol. I, p. 135.
Major, R. H., and Curran, E. J. (1925). *Journ. Amer. Med. Assoc.*, Vol. LXXXIV, p. 674.

is apparently a latent power of all vibrios and of no absolute value in differentiation of vibrios.

Class II. *Vibrios not agglutinable by cholera specific serum.*

A. *Non-cholera vibrios.*—Vibrios that differ markedly in their properties from the true cholera vibrio and which can be isolated in places where cholera does not exist or has not been for a number of years. This group includes the phosphorescent, chromogenic, non-proteolytic, non-saccharolytic vibrios and other vibrios that have no connection whatsoever with the cholera vibrio. These will not be considered further here.

B. *Atypical cholera vibrios.*—This group includes the vibrios referred to as cholera-like or paracholera vibrios and several of the vibrios that have received specific names. They abound in nature where cholera exists or has recently existed and can be frequently isolated from cholera convalescents, either alone or together with typical cholera vibrios. They are all monoflagellate and motile, they produce indol, liquefy gelatine and give the sugar reactions of the standard cholera vibrio. They differ from the true cholera vibrio in their serological reactions. They themselves do not belong to one serological group. Cross agglutination tests between various atypical vibrios give evidence of a large series of groups which are distinctly differentiated serologically. Greig (1917) found twenty-two serological groups amongst 78 strains of cholera-like vibrios that he examined.

The aetiological significance of the atypical vibrios is still undetermined. It is the want of serological identity of the atypical vibrios with the true cholera vibrio which has led to their being distinguished from the causative organism of the disease. A further difficulty is that as man alone is susceptible to cholera we have no means as yet of determining the presence or absence of virulence in a vibrio. The identity or non-identity of these atypical vibrios with the true cholera vibrio has been the subject of numerous investigations. Although on the subject of the serological variations of vibrios, brought about either by subculture alone or by subjection to other experimental biological

occurring in the specific serological reactions is so deeply rooted in the minds of bacteriologists that many authors emphatically deny either the possibility of the loss of agglutination of a cholera vibrio or that the transformation of a non-agglutinating vibrio to an agglutinating vibrio can ever take place. They hold that such observations are due either to errors in technique or are the results of uncritical investigations and are based on purely theoretical grounds. The nature of the experiments devised to alter the serological characters of a vibrio were such that they did not yield uniform and convincing results. Many investigators, although following the original technique of those who had reported success in bringing about variations in the property of agglutination of a vibrio, found it impossible either to transform a true agglutinable cholera vibrio into an in-agglutinable atypical vibrio or to convert a cholera-like vibrio into a typical agglutinable vibrio. The cause of failure to confirm the results of the variations of agglutinability was due not to faulty technique but, as suggested later by d'Herelle, to the difference in the vibrio itself—the presence or absence of contaminating bacteriophage in the vibrio or the possibility of contamination by bacteriophage in the course of the experiment.

d'Herelle, Malone and Lahiri (1930) were the first to present convincing experimental proof that the property of agglutinability by a specific high-titre serum, which alone distinguishes true cholera vibrio from the so-called cholera-like vibrios, was variable and could be lost. They showed that certain strains of vibrios agglutinable at maximum titre when first isolated became inagglutinable after successive subcultures *in vitro*, and they presented conclusive experimental evidence that such changes are the result of infection of the cholera vibrio by bacteriophage. They summarized the results of the variability of the character 'agglutinability' as follows:—

'Cholera vibrios undergo profound modifications in the intestine of patients the principal stages of which are indicated in the following table, but all intermediate stages are possible because experiments show that the different characters vary independently of one another.

Motility	Morphology	Fermentations	Reduction of nitrates	Hæmolytic power	Agglutination	Virulence
+	Normal	Normal	+	+	+	+
+	Normal	Normal	+	+	+	—
+	Normal	Normal	+	+	—	—
+	Normal	Normal	+	—	—	—
+	Normal	Normal	—	—	—	—
+	Normal	Abnormal	—	—	—	—
+	Abnormal	Abnormal	—	—	—	—
—	Abnormal	Abnormal	—	—	—	—

conditions, a mass of literature has accumulated, the belief as to the impossibility of any change

The fact that the various germs possessing characters of such diversity truly constitute real

mutations of the typical cholera vibrio is beyond dispute for similar mutations can be obtained *in vitro* by the action of the bacteriophage'.

We have already shown (Pasricha, de Monte and Gupta, 1931) that the secondary growths that develop after the action of the bacteriophage isolated from a convalescent cholera patient on an agglutinating and phage-sensitive ultra-pure vibrio isolated from the same case are variable in their agglutinability. Non-agglutinating colonies can be isolated from such phage-infected cholera vibrios, whereas in the secondary colonies that develop after the action of laboratory cultures of cholera phage (at that time cholera phage types A, B and C only were known) on freshly isolated cholera vibrio or on laboratory strains, serological mutations could not be so readily obtained. We have repeated these experiments several times and have fully confirmed these findings. With the other types of cholera phage, particularly with types G and H it is comparatively easy to bring about the loss of agglutinability in an agglutinating cholera vibrio. The results of some recent experiments on the effect of bacteriophage on the agglutinability of cholera vibrio are summarized below :—

variant forms of the true cholera vibrio. It becomes, therefore, of the greatest importance to establish whether, under any conditions, the non-agglutinating atypical vibrio can become the agglutinating typical cholera vibrio. d'Herelle throughout his writings and d'Herelle, Malone and Lahiri (1930) stress that when the loss or the modification of a character is the result of a mutation, as for example, the loss of agglutinability of a cholera vibrio by the action of bacteriophage, this character cannot be recovered. The mutation appears to be final and the return to the original form impossible. In discussing the problem of endemicity of cholera they express the opinion that while in epidemic regions degenerated vibrios never recover their virulence, in endemic regions recovery can occur. The unknown factor responsible for the 'regeneration' that occurs in endemic centres of the disease must be of the nature of a living organism present in the waters. They suggest that certain aquatic animals peculiar to Bengal and Indo-China—the endemic centres of cholera—may be concerned; some annelid, crustacean or mollusc in the intestine of which the cholera vibrio can live for a long time and more especially in the intestines of

Serological changes induced in true cholera vibrios after infection with cholera phage (mixed types A, B, C, D, E, F, G, H, J and K)

Titre of agglutination of the strains of vibrios tested	AGGLUTINATION OF SECONDARY GROWTHS WHICH DEVELOP AFTER ACTION OF CHOLERA PHAGE					
	Number of strains tested	Number of strains in which titre of agglutination was unchanged	Number of strains in which titre reduced to half of original	Number of strains in which titre reduced to less than 1/6th of original	Number of strains inagglutinable by cholera serum	Number of strains in which agglutination increased as compared with the original
1 in 6,000 and over ..	29	5	5	5	14	..
1 in 2,000 to 1 in 6,000 ..	16	6	1	1	8	..
1 in 1,000 to 1 in 2,000 ..	5	1	1	3
Less than 1 in 1,000 ..	2	2
TOTAL ..	52	12	6	6	23	5

Of the fifty-two strains of agglutinating cholera vibrio after the action of mixed cholera phage twelve strains show no change in the titre of agglutination, twelve show definite diminution in the property of agglutination and twenty-three, or forty-four per cent, show complete loss of agglutinability. It is interesting to note that out of seven strains of vibrios originally only partially agglutinating the secondary growths of five strains show increased agglutinability.

A number of investigators have recorded the finding of atypical vibrios in waters in association with outbreaks of cholera more particularly towards the end of an epidemic, and that such vibrios are not found in places which have been free from cholera for some years. The experimental evidence of the loss of agglutination by a cholera vibrio under the influence of bacteriophage is so conclusive that it can be reasonably concluded that most, if not all, of the atypical vibrios found in places where cholera exists are

which the avirulent cholera vibrio can become regenerated.

We have already shown (Pasricha, de Monte and Gupta, 1931) that twenty per cent of 355 strains of cholera-like vibrios isolated from waters and man in Calcutta were lysable by ultra-pure races of cholera phage (types B and C). The secondary colonies that develop after the action of cholera bacteriophage on cholera-like vibrios in some experiments are agglutinable by cholera specific serum. They completely

teriophages which we have called cholera-like vibriophages, or vibriophages, in contra-distinction to the pure-line cholera phages. These vibriophages can lyse certain strains of non-

The diagram illustrates the genetic relationships and phage adsorption patterns of various Ag and NaAg strains. At the top, a 'Cholera phage' is shown with a black dot. Below it, various Ag and NaAg strains are listed, including 'EL Tor Type', 'Less Ag', and 'NonAgglutinating'. Lines connect these strains to a series of phage adsorption patterns at the bottom, which are labeled 'Cholera-like Vibriophage'. The diagram illustrates how different Ag and NaAg strains interact with different phages, leading to various adsorption patterns.

Agglutinating "ultra-pure" cholera vibrio (non-hæmolytic).

Agglutinating phage infected cholera vibrio.

Partially agglutinable with cholera high titre serum.

Not agglutinable with cholera high titre serum.

Hæmolytic.

*Cholera*phage.

Cholera-like vibriophage.

agglutinating vibrios, and the resulting secondary growths of some vibrios are both agglutinable by cholera serum and lysable by pure-line choleraphages, and are thus indistinguishable

from true cholera vibrios. These experiments have been repeated several times and the previous results confirmed. The results of the examination of fifty-six recently-isolated strains of non-agglutinating vibrios is given below:—

Changes induced in the serological reactions of atypical non-agglutinating vibrios after the action of bacteriophage

Total number of atypical non-agglutinating vibrios examined ..	56
Agglutination reaction unchanged after the action of bacteriophage in ..	32
Number of strains that became agglutinable after the action of cholera-phage ..	11
Number of strains that became agglutinable after the action of vibriophages ..	13
Total number of strains that became agglutinable with cholera serum after the action of bacteriophages ..	24 or 43 per cent.

We have experimental evidence, therefore, that in regions like Calcutta where cholera is endemic there exist bacteriophages under the influence of which, in the laboratory, certain strains of atypical non-agglutinating vibrios can acquire the property of agglutination with cholera specific serum. We have looked for the presence of such bacteriophages in the waters of places where cholera is not endemic. We have examined 150 samples of waters collected at Hardwar and about 100 samples of waters from Kurseong and failed to find such vibriophages. We have not made a sufficiently extensive study of vibrios and phages in non-endemic areas, nor have we made an investigation into the seasonal variations of vibriophages in relation to the epidemic of cholera, to enable us to draw definite conclusions as to the part played by vibriophages in the epidemiology of the disease, but in the laboratory under the influence of a virus disease (cholera-phage) the typical cholera vibrio becomes an harmless saprophytic organism which when once again parasitized by another virus disease (vibriophage) assumes the characteristics which render it indistinguishable from the typical virulent type. That recovery from a chronic disease following infection by another acute disease can take place is not without parallel in medicine. Whether the vibrios regain their virulence or not we have no means of judging. The conclusion is forced upon us that the vibriophages play an important part in the epidemiology of cholera and that they are one of the important factors in bringing about a regeneration of degenerated cholera vibrios.

A schematic representation of the variations undergone by a smooth agglutinating cholera vibrio after the action of bacteriophage is given. We prefer to use the term variants instead of mutants, as the latter term, often loosely

applied, implies irreversible change of characteristics. Doorenbos (1932) recently published a similar diagram but the relationship of the atypical vibrios to the cholera vibrio was not illustrated in the diagram. The variants of cholera vibrio obtained *in vitro* are much more variable in their character than those represented in the diagram which represents the peaks of variability and illustrates the probable relationship of the five great classes of vibrios:—

1. *True cholera vibrio, agglutinable by specific cholera serum.*—In the diagram this vibrio is represented as being non-hæmolytic. We have already said that cholera vibrios show wide variations in their ability to produce hæmolysins and that many strains of cholera vibrio cause rapid lysis of red blood cells. We have shown the cholera vibrio as non-hæmolytic as a contrast to the other vibrios which are frankly hæmolytic.

2. *The hæmolytic agglutinating vibrios—the so-called El Tor vibrios.*—Although we have not isolated vibrios of this type from cholera cases in India, it can be experimentally produced in the laboratory.

3. *Vibrios partially agglutinable by cholera serum.*—This group is a very important one for the study of variants of cholera vibrio.

4. *Vibrios not agglutinable by cholera serum.*—Vibrios of this type can be frequently isolated in nature. They are the aberrant forms of cholera vibrio and do not form an homogeneous serological group. These we referred to as atypical cholera vibrios. The secondary colonies that develop after the action of vibriophages on these vibrios are agglutinable by cholera serum and are indistinguishable from the true cholera vibrio by cross agglutination and absorption tests.

5. *Finally, the 'G' type, small coccid forms which are filter-passers and later develop into vibrios.*—The ætiological significance of these forms is still undetermined.

REFERENCES

- d'Herelle, F., Malone, R. H., and Lahiri, M. N. (1930). Studies on Asiatic Cholera. *Indian Med. Res. Memoir No. 14*, p. 57.
- Doorenbos, W. (1932). *Étude sur la Symbiose de Vibrión Cholérique avec le Bactériophage*. Alexandrie: Société de Publication Egyptiennes.
- Greig, E. D. W. (1917). Bacteriological Studies of Cholera-like Vibrios Isolated from the Stools of Cholera Cases in Calcutta. *Indian Journ. Med. Res.*, Vol. IV, p. 658.
- Inouye, and Kakihara, T. (1925). *Sci. Report Govt. Inst. Infect. Dis., Tokyo Imp. Univ.*, Vol. IV, p. 17.
- Pasricha, C. L., de Monte, A. J., and Gupta, S. K. (1931). Mutations of Cholera-like Vibrios under the Action of Bacteriophage. *Indian Med. Gaz.*, Vol. LXVI, p. 610.
- Pasricha, C. L., de Monte, A. J., and Gupta, S. K. (1931). Cholera and Cholera-like Vibriophages. *Ibid.*, Vol. LXVII, p. 487.

PLATE IX



Fig. 1.—Photomicrograph showing a spirillum in the nasal smear of a leper. Combined Leishman's and Giemsa's stain. (Magnification $\times 1,200$ approx.)

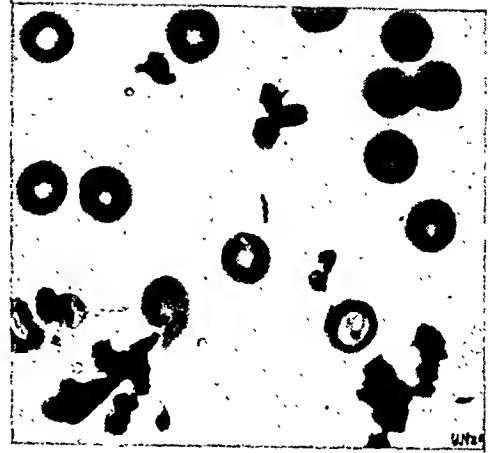


Fig. 2.—Photomicrograph showing spirillum in the blood of a mouse infected from the leper. Combined Leishman's and Giemsa's stain. (Magnification $\times 800$ approx.)

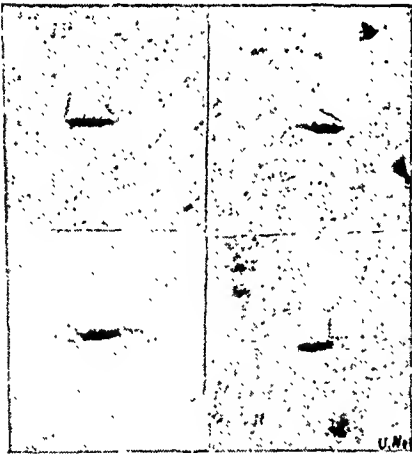


Fig. 3.—Photomicrograph of the spirilla. Showing terminal flagella in the peritoneal exudate of the mouse infected by subinoculation from the guinea-pig. Tribondeau's modification of Fontana's stain. (Magnification $\times 1,200$ approx.)

Owing to the deposition of silver the spirilla look much thicker than they would appear when stained by Romanowsky stains.



Fig. 4.—Photograph of the lesion following the injection of infected blood from a mouse into the arm of volunteer I.

EXPERIMENTAL STUDIES WITH A SPIRILLUM FOUND IN THE NASAL CAVITY OF SOME LEPERS

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WHILE examining the nasal smears for lepra bacilli as a routine diagnostic measure, one of us (S. N. C.) found a spiral organism characterized more or less by its uniformity of shape and size though an occasional individual was larger than others. A few months later a similar organism was found in another case.

A saline emulsion of the scrapings was examined under dark-ground illumination. The organism showed the typical darting movements of a spirillum as distinct from those of a spirochete. Some of the emulsion was injected intraperitoneally into a white mouse which died apparently of sepsis within 48 hours. As the case was lost sight of, no further experiments could be made until in December 1932 we got a third case showing a fairly heavy infection with the spirillum.

This patient has been under our observation for more than 5 months. During this period eleven tame mice have been inoculated with the emulsion of nasal scrapings on different dates. On most of these occasions spirilla could be demonstrated either in stained smears or by examination by dark-ground illumination. Out of these eleven mice nine died apparently of sepsis within 3 days of inoculation. On post-mortem examination performed within two hours of death one showed pneumococci in abundance in the smears of the heart blood. Of the surviving mice one showed spirilla in the blood and the other died 13 days after inoculation; on post-mortem examination of the latter no spirilla were detected in the heart blood or spleen smears.

To eliminate the possibility of spontaneous infections of *S. minus* in the laboratory mice, as reported by Robertson (1930), two young guinea-pigs were injected with the nasal scrapings containing a fair number of spirilla (one in every 5 or 6 microscopic fields).

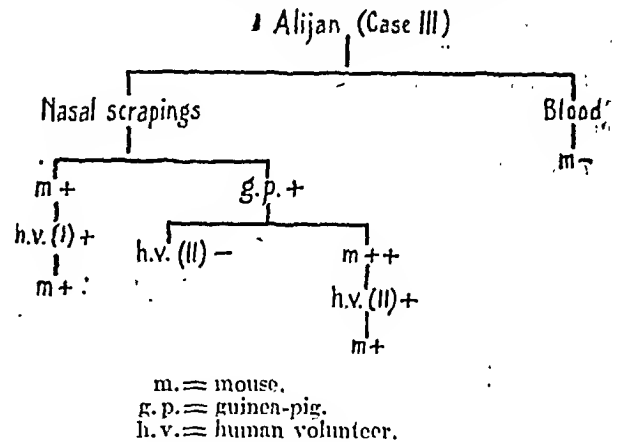
Both these animals showed scanty infections on the 16th and 23rd days, respectively.

A white mouse subpassaged from one of these guinea-pigs showed a heavy infection (spirillum found in almost every field) as early as the 8th day.

Inoculation of human volunteers

1. Sweeper B, aged 40, was given an injection into the skin of the arm of 0.1 c.cm. of blood of the mouse infected by inoculation of nasal scrapings of case no. III.

Table showing the infectivity of nasal scrapings and blood of Alijan (case III) to different hosts.



After the inoculation he was kept under observation. No sign of inflammation at the site of injection was noticed till the 8th day. On the next day, however, the part became markedly swollen and oedematous. The axillary glands of the corresponding side were enlarged and tender. He complained of severe headache. There was high fever.

The exudate obtained by puncturing the oedematous area showed no spirilla but the blood taken at the height of fever on the 9th and 10th days and injected into mice produced infection in these animals.

On the 3rd day of the fever (or the 12th day of inoculation) an injection of 0.3 gm. novarsenobillon was given which resulted in the fall of temperature, and the local oedema and lymphadenitis subsided in a few days. The temperature has been normal since then.

2. An inmate of the Gobra Leper Asylum volunteered for inoculation. His nasal scrapings were examined before experimental inoculation. There were no spirilla, but a large number of acid-fast bacilli were present.

A few drops of blood from one of the infected guinea-pigs were inoculated into the back of the arm. As there was no evidence of local inflammation or fever till the 11th day, he was given another injection of the blood from a mouse sub-inoculated from the same guinea-pig. On the 8th day from the time of the second injection he developed a typical local lesion, fever and rash on the chest and abdomen. A mouse passaged on the 2nd day of fever was positive for spirilla.

Brief account of the leprosy cases who showed spirillum in the nasal smears

Four such cases have been encountered out of over 3,000 cases examined in the course of about 3 years.

Case I.—Hypopigmented anaesthetic patch on the left side of the abdomen. Gave history of rat bite about 25 years ago, but could not recollect whether he had developed rat-bite fever.

Case II.—Anaesthetic patch on the leg. No history of rat bite.

Case III.—Hypopigmented anæsthetic patch on the left leg. On several occasions the nasal smears were positive for spirilla. The last positive smear was that of 12th May, 1932. He gave no history of rat bite, but complained of irregular fever off and on.

Blood was not infective to mice, but inoculation of nasal scrapings produced infection in mice and guinea-pigs.

Case IV.—Gave no history of rat bite. Showed a fair number of spirilla in the nasal smears.

CHART I
Volunteer II.

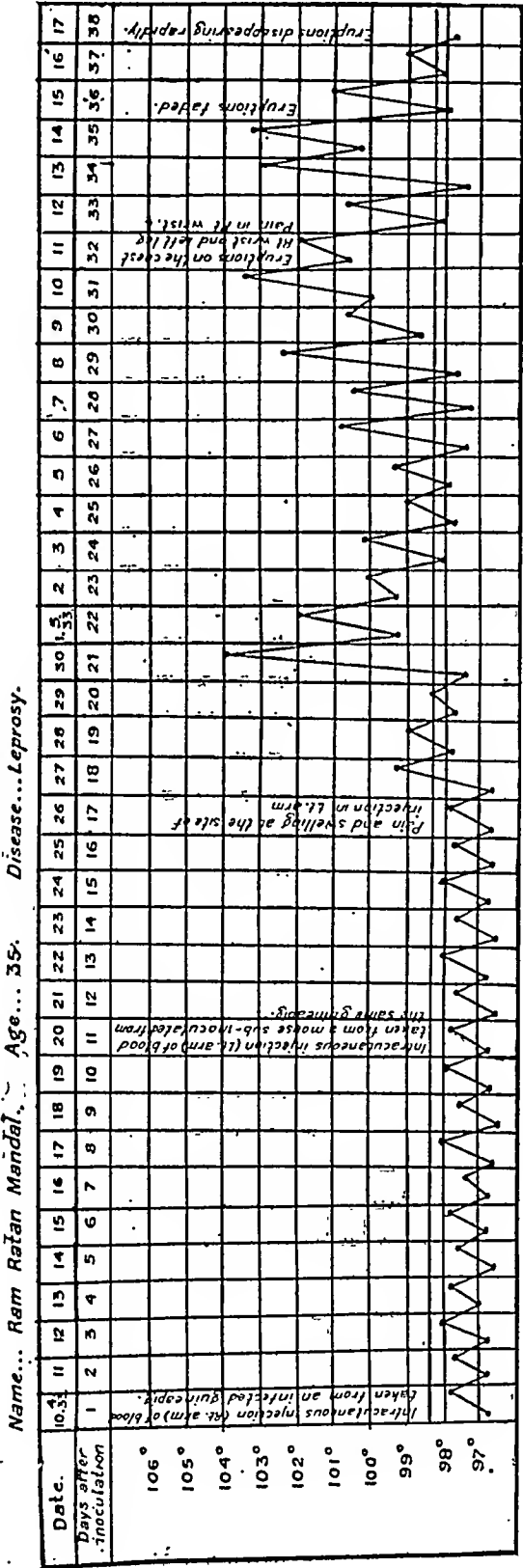
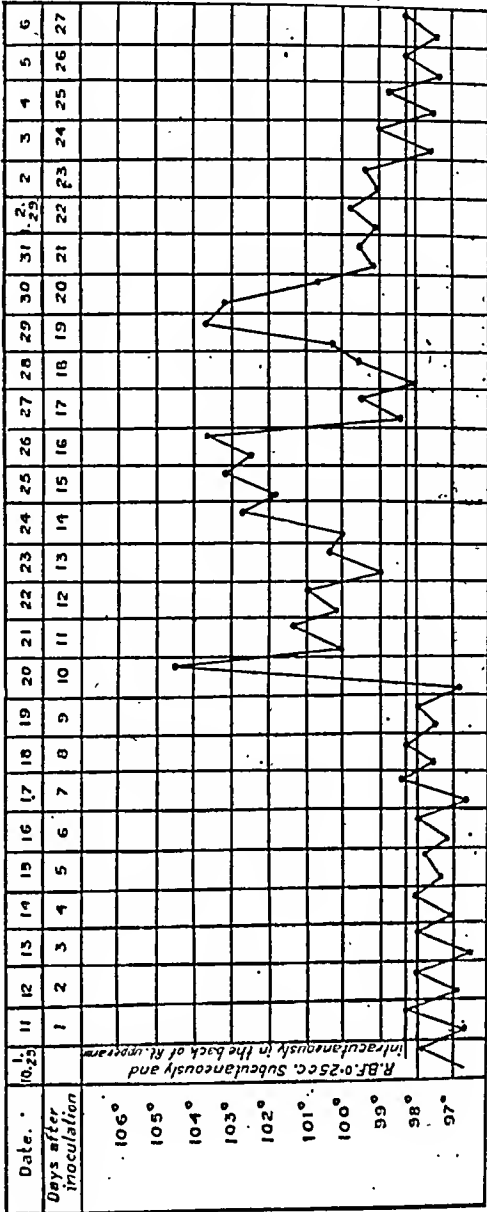


CHART II

TEMPERATURE CHART OF A LEPER EXPERIMENTALLY INFECTED WITH *SPIRILLUM MINUS* AS A THERAPEUTIC MEASURE.
Name... Hafiz uddin. Disease... Leprosy.



CANCERUM ORIS IN A MONKEY INFECTED WITH *LEISHMANIA DONOVANI*

By R. O. A. SMITH, D.T.M., I.M.D.

Kala-azar Enquiry, Indian Research Fund Association,
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THE object of this note is to report the occurrence of cancrum oris in a monkey (*Macaca irus*). It is believed that this is the first occasion on which this complication has occurred in an experimental animal infected with *Leishmania donovani*.

The previous history of this monkey is that it had been given a malarial infection in the series of experiments reported by Drs. Napier and Campbell (1932) and that, after the necessary data regarding malaria had been obtained, it had been handed over by Dr. Napier for leishmania infection experiments.



Head of a monkey (*Macaca irus*) showing cancrum oris.

The monkey was injected subcutaneously into one of its limbs with one cubic centimetre of an emulsion of leishmania-infected hamster liver and spleen on 7th June, 1932. A copper wire was immediately tied above the site of

(Continued from previous page)

think of any reason why the spirilla should have a particular liking for nasal mucous membrane.

We are indebted to Lieut.-Col. H. W. Acton, C.I.E., I.M.S., and Dr. E. Muir, M.D., F.R.C.S., for their invaluable help during the investigation.

REFERENCE

Robertson, A. (1930). *Spirillum minus*. Carter, 1887, The *Ætiological Agent of Rat-bite Fever: A Review*. *Ann. Trop. Med. and Parasit.*, Vol. XXIV, p. 367.

inoculation to produce venous congestion of the limb, in the hope that the leishmania would be more readily taken up by the leucocytes in the congested area. This was one of a series of six monkeys which were treated in the same way, and was one of two that became infected with leishmania.

Four months after the inoculation a necrotic process, typically sudden in onset and development, occurred; a swelling was noted one day and the next morning the cheek had ulcerated and sloughed, exposing the bones of the face. The photograph of the head of the animal shows the lesion. The animal was killed, as it would certainly have died within a very short time. A heavy leishmania infection of the spleen and liver was found.

The intensity of infection in experimental monkeys of this species has varied considerably—some being very susceptible and showing quite heavy infections and others not showing any infection at all. In view of the occurrence of this complication, which suggests that in this animal the infection ran a course similar to that occurring in man, it is unfortunate that this was not one of the animals in which an accurate cytological study was made, as it is possible that some changes might have been detected which would have explained the production of an infection of this nature in this particular animal.

REFERENCE

Napier, L. E., and Campbell, H. G. M. (1932). Observations on a *Plasmodium* infection which causes hæmoglobinuria in Certain Species of Monkey. *Indian Med. Gaz.*, Vol. LXVII, p. 246.

'VINCENT'S DISEASE' IN A *MACACA IRUS* MONKEY

By K. V. KRISHNAN, M.B., B.S., M.R.C.P.E.,
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(From the Kala-Azar Enquiry, Indian Research Fund Association, All-India Institute of Hygiene and Public Health, Calcutta)

CERTAIN necrotic and gangrenous infective processes, such as ulcero-membranous stomatitis, hospital gangrene, noma, and gangrenous laryngitis, in which spirochaetes and fusiform bacilli are found, occur in human beings and go by the name of Vincent's disease. As far as the writer is aware neither these lesions nor these organisms have been recorded in experimental animals. A *Macaca irus* monkey that was being used in kala-azar transmission experiment developed a peculiar inflammatory condition of the palate and nose, characterized by multiple sinuses and a sanguino-purulent fetid discharge. Examination of the pus from the sinuses, both by dark-ground and in stained smears (Giemsa and Fontana), revealed the presence of spirochaetes

and fusiform bacilli. Inoculation of this pus into mice subcutaneously, caused the death of the animals within 24 to 48 hours, after producing extensive local necrosis at the site of inoculation. In the material from the necrosed area in the mice, streptococci and fusiform bacilli were found but not spirochaetes; the internal organs of these animals showed no infection. The history of the monkey in question is as follows:—

It had suffered from an attack of inoculation malaria from 19th December, 1931, to 17th February, 1932, and had proved refractory to subsequent inoculation on 26th July, 1932, and 5th August, 1932; it had received in addition on 6th August, 1932, a small dose (0.1 c.cm.) of *Leishmania donovani* (flagellate culture) subcutaneously. Four months later (8th December, 1932) liver puncture was done on the animal and the material obtained examined for *L. donovani* with negative results. The monkey was being kept under observation when it showed the above-mentioned suppurative condition (first noticed on 7th January, 1933).

The monkey has now had the disease for the past four months, and although the local condition has been slowly and steadily getting worse there has only been very slight constitutional disturbance. Examination of spleen-puncture material from the monkey showed *L. donovani* on 28th April, 1933.



The points of interest about this finding are—

(1) that a gangrenous suppurative process allied to cancrum oris occurs in the course of leishmania infection in *M. irus* monkeys;

(2) that this condition is associated with the presence of fusiform bacilli and spirochaetes.

A photomicrograph of the spirochaetes and fusiform bacilli is given.

THE FILTRABLE PHASE OF THE TUBERCLE BACILLUS

By M. B. SOPARKAR, M.D.

(Officer-in-Charge, Tuberculosis Inquiry, Indian Research Fund Association)

and

SUB-ASSISTANT SURGEON JEMADAR CHANCHAL SINGH DHILON, I.M.D.

(From the Haffkine Institute, Parel, Bombay)

(Preliminary Note.)

A CONSIDERABLE amount of experimental work has been done on this aspect of the life history of the tubercle bacillus during the last ten years and two opposite views are at present held on the question of the filtrability of the tubercle bacillus. One group of observers claim to have proved by experiment the existence of a filtrable form of this bacillus, while another group of workers, having obtained no positive results, are unable to support this claim.

With a view to elucidating this problem experiments on this subject were commenced in 1928. This note deals with some of the main findings of these experiments.

The lines of work adopted consisted of obtaining filtrates of tuberculous material that had been passed through porcelain candles, inoculating them into animals and studying the results of these inoculations.

The material used for filtration consisted of tuberculous sputum (six experiments) and tuberculous tissues of laboratory animals infected with known bovine bacilli (four experiments). Suspensions of the material in saline were filtered through Chamberland L₃ candles, and inoculated subcutaneously into guinea-pigs. In these ten experiments passages were made from guinea-pig to guinea-pig with emulsion of lymph glands and spleens of the previously inoculated animals which were killed at regular intervals and carefully examined for the presence of acid-fast bacilli. These were detected in the whole series in 66 out of 190 animals examined—the positive results being found in different stages of the passage but not uniformly. No typical naked-eye lesions of tuberculosis were, however, detected in any of these animals.

The mere finding in the inoculated guinea-pigs of acid-fast bacilli, however, was not regarded as sufficient evidence of the existence of a filtrable phase, and these were further successfully cultivated and pure growths were obtained in six out of ten experiments. Four of these strains were studied as to their character and all of them were found to differ, both culturally as well as in their pathogenicity, from the strains of bacilli present in the original material used for filtration.

In the first two experiments in which the material used was tuberculous sputum, while the original bacilli possessed characters of the human type, the cultures obtained from the

tissues of animals treated with the filtrates behaved differently—in one instance it resembled the avian type and in the other it was avirulent both for the guinea-pig as well as for the fowl.

In the other two experiments with the tissues of guinea-pigs in which the animals were infected with tubercle bacilli of the bovine type, results with the 'filtrate cultures' were similar to those just described, i.e., these cultures instead of showing characters of the original bovine type behaved like the avian type. In one of these experiments also, the culture derived from an earlier passage animal had not attained the virulence for the fowl acquired by another culture of the same experiment but obtained from a later passage animal—suggesting a gradation. In the rabbit the lesions produced by the latter strain closely resembled those caused by the avian bacillus.

These results seem to indicate not only that there exists a filtrable phase of the tubercle bacillus, but, what is even more interesting, that there is a biological change in the character by which, when suspensions of sputum or of animal tissues containing the human or the bovine type of tubercle bacilli having been passed through a porcelain filter and the filtrates subsequently through bodies of guinea-pigs, the acid-fast bacilli recovered from their tissues are successfully cultivated, these cultures are found no longer to possess the virulence of the original strains for this animal and in some cases to behave like the avian bacillus.

This change in the biological character of the strains isolated from the passage guinea-pigs treated with the filtrates—their avirulence for this animal—may perhaps furnish a possible clue to the finding of atypical tuberculosis by some observers in guinea-pigs inoculated with the filtrates, and also to the negative results of other workers adjudged by the absence in the inoculated animals of signs of classical tuberculosis anticipated when dealing with material containing human or bovine types of bacilli.

THE CONSTANCY OF THE SUGAR-CHLORIDE RELATIONSHIP IN DIABETIC URINES

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In going through my old records of the analyses of a large number of samples of diabetic urine examined during the last 16 years, I found that a close relationship appeared to exist between the elimination of chlorides and elimination of sugar in urine. The elimination of sugar appeared to have taken place at the expense of that of other solids, chiefly the chlorides, and it struck me that a suitable formula to express the sugar-chloride relation might be worked out.

The formula I adopted is as follows:—

$$\text{Percentage of sugar} = \frac{G - (Cl \times 10)}{4.4}$$

where G = the last two figures of the specific gravity taken at 15°C.

Cl = percentage of chlorides expressed as NaCl.

For example, if the corrected specific gravity were 1.035 and the chlorides 0.25 per cent, the sugar percentage could be calculated as $\frac{35 - (0.25 \times 10)}{4.4}$ or 7.38 per cent.

It is obvious that the specific gravity should be taken very carefully with a reliable urinometer. All urinometers are standardized at 15°C., that is, they indicate 1,000 in distilled water at the temperature of 15°C.

It is however not necessary to take the specific gravity of the urine at this temperature, if a correction is made. The specific gravity is lowered by 0.001 for each 3 degrees above 15°C., so that if the urine temperature is 27°C., $\frac{27 - 15}{3}$,

or 4, must be added to the urinometer reading to bring it to the true specific gravity.

The estimation of chlorides can be done volumetrically with standard silver nitrate solution and potassium chromate as indicator; this method is sufficiently accurate for the purpose. The standard silver nitrate solution is made by dissolving 29.235 grammes of pure and dry crystals of silver nitrate in a litre of water at 15°C.; one cubic centimetre of this solution is equivalent to 10 milligrammes of sodium chloride. The estimation is made as follows: 10 c.cm. of urine is taken in a flat-bottomed porcelain dish and diluted with about 25 c.cm. of distilled water and then titrated with silver nitrate solution with about 0.5 c.cm. of 10 per cent potassium chromate solution as indicator. Supposing 6 c.cm. of the standard solution were required for the titration, the percentage of chlorides would be 0.6, if 13 c.cm. were required the percentage would be 1.3, and so on. The process is very rapid, takes about two minutes to perform, and is fairly accurate for clinical purposes.

Now with the above data, it is a question of a few seconds to calculate the percentage of sugar. The formula gives the percentage of sugar quite accurately, the difference between the calculated figure and that obtained by actual titration with the Benedict reagent not exceeding 0.5 per cent. It has been observed that if the secretion of urine is profuse and the colour is pale straw, such as is usually met with in advanced cases of glycosuria having large amounts of sugar, the result obtained by this method is particularly accurate; but if the case is complicated with any form of nephritis, in early cases of glycosuria passing small quantities of sugar, in cases with high-coloured urine, and in the presence of excess of urates or phosphates,

the chloride-sugar equilibrium is disturbed and the result is not satisfactory. The best result is obtained in the urine of patients who suspect something wrong with them and come to the doctor for treatment for the first time, but as soon as they are put on a restricted diet, the amount of sugar begins to come down steadily and the result becomes progressively inaccurate and subsequently a condition is reached when the formula becomes unworkable. If the treatment is stopped and the patient indulges in indiscretions in his diet, his condition gets worse

and the chloride-sugar equilibrium is again restored.

The object of publishing this preliminary note is to elicit suggestions for working out a more comprehensive formula which would eliminate the various sources of error caused by urea, urates, phosphates and other interfering substances.

The following is a statement of cases selected from my records to show the normal and complicated cases of glycosuria which have been referred to in the paper :—

Number	Corrected specific gravity	Percentage of chlorides	Percentage of sugar calculated from the formula	Percentage of sugar by actual estimation	Difference between the two results in per cent	REMARKS
1	1.022	0.12	4.72	4.71	+ 0.01	
2	1.029	0.38	5.73	5.80	— 0.07	
3	1.030	0.40	5.90	5.90	Nil	
4	1.016	0.60	2.27	2.35	— 0.08	
5	1.032	0.15	7.0	7.1	— 0.10	
6	1.033	0.45	6.47	6.6	— 0.19	
7	1.026	0.30	5.22	5.30	— 0.08	A trace of albumin and a few granular casts.
8	1.034	0.15	7.40	7.50	— 0.1	
9	1.034	0.26	7.22	6.80	+ 0.42	Excess of phosphates.
10	1.034	0.32	7.0	7.20	— 0.20	
11	1.027	0.4	5.2	4.9	+ 0.3	
12	1.034	0.24	7.18	7.0	+ 0.18	
13	1.038	0.10	8.41	8.50	— 0.09	
14	1.032	0.50	6.10	5.40	+ 0.70	Excess of urates.
15	1.029	0.30	6.0	4.3	+ 1.7	Nephritis with much albumin and casts.
16	1.025	0.10	5.45	2.85	+ 2.60	Abundance of phosphates and urates.

GAVANO

A NEW SPECIFIC FOR AMOEBIC DYSENTERY

By G. H. FITZGERALD, M.R.C.S., L.R.C.P. (Lond.),
D.T.M. & H. (Lond.), D.P.M. (Cantab.)

MAJOR, I.M.S.

Civil Surgeon, Aligarh, U. P.

GAVANO is a new synthetic preparation, prepared by Bayer, and is said to have a specific action on the *Entamoeba histolytica*. No details as to its chemical composition are at present available. It is put up for use both in the form of tablets for oral administration, and in ampoules containing a 0.5 per cent solution for intramuscular injection. I have only used the former, which contain 0.25 grammes of the active product. The course recommended is one to three tablets daily for six days, though this can be increased without ill effects; a second course is given after a week's interval. My practice has been to administer two tablets daily for ten days, the usual dose of castor oil being given at the start.

The makers claim for it that :—

(1) It produces no vomiting.

(2) It is far less toxic than emetine, the therapeutic index tested by injections into cats being 1:3.

(3) There is no cumulative action.

(4) Through its action on the medullary centres it causes a lowering of blood pressure and diminishes CO₂ elimination; this increases vagal activity and results in increased peristalsis of the large intestine.

(5) It has proved to be remarkably effective in the treatment of amoebic dysentery in cats, a condition which is unaffected by emetine.

As I myself had suffered for some years from chronic amoebic dysentery and hepatitis, a condition which necessitated almost constant dosage with stovarsol and occasional courses of emetine to keep in check, I took one course of twenty tablets. This is now over twelve months ago, and I have had no return of the old symptoms and several stool examinations have been completely negative, though these had been positive on numerous previous occasions despite treatment. During the course, I noted a tendency to looseness of the bowels and some dyspnoea, though this was not sufficient to prevent active exercise throughout. It has unfortunately only been possible to give it a limited clinical trial; the following cases, typical of others, may be quoted.

Case I.—Boy aged 18. Had severe amoebic dysentery with about 17 stools daily. Active *Entamoeba histolytica* seen. Placed on Gavano, one tablet twice daily. On the third day the motions were reduced to 4, and traces only of mucus and blood were seen. At the end of seven days the motions were completely normal and two in number only. At the end of ten days he was discharged as cured. The stools were repeatedly examined for three months after and no *Entamoeba histolytica* or cysts were found, and he remained free of symptoms.

Case II.—Man aged 25. Gave a history of passing blood and mucus for the past three months. Active *Entamoeba histolytica* found in the stool. Was given the Gavano course combined with bismuth. After four days the number of motions was greatly reduced, pain had disappeared, and the stools were almost normal in appearance.

He was discharged three weeks after admission, apparently perfectly well, stool examination being negative.

Case III.—Male aged 35. History of passing blood and mucus for 15 days, and pain in the right hypochondrium. Active *Entamoeba histolytica* found. Through a misunderstanding he was given one pill only for seven days, combined with bismuth. Nevertheless, at the end of that period he was passing one motion a day only and all his symptoms had disappeared. He absconded on the eighth day and no further stool examinations were therefore performed.

Case IV.—Male aged 60. Admitted with a large fluctuating swelling the size of a melon in the epigastrie region, which was obviously shortly going to burst.

He was greatly emaciated. The abscess was opened and about three and a half pints of chocolate-coloured pus evacuated. There was very extensive destruction of liver tissue. He was placed on Gavano treatment, and, beyond irrigation of the abscess cavity with saline, nothing else was done. Sixteen days later the discharge had almost entirely ceased, and the wound was healthy and healing rapidly.

Unfortunately at this stage he developed acute lobar pneumonia and died three days later. The ready healing of the wound in a much debilitated subject was most remarkable.

In no case in which I have tried it has Gavano failed to relieve the symptoms of amoebic dysentery, and this without causing the patient any of the discomforts associated with any of the recognized forms of emetine treatment. Nausea is unknown.

To what extent it is capable of permanently eliminating the *Entamoeba histolytica*, it is impossible as yet to say.

My own experiences with it have been so favourable that I feel justified in drawing attention to its possibilities.

My thanks are due to the Haverro Trading Company Ltd. in Calcutta, who kindly supplied me with the drug for this clinical trial.

A Mirror of Hospital Practice

DOUBLE PAPILLOEDEMA FOLLOWING ANTIRABIC INOCULATION: RECOVERY

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LIEUTENANT-COLONEL, I.M.S.

Ophthalmic Surgeon, General Hospital, Rangoon, and
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and

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LIEUTENANT-COLONEL, I.M.S.

Director, Pasteur Institute of Burma, Rangoon

On the 6th April, 1932, a healthy-looking Anglo-Indian lady, aged 31, came to see one of us (H. S. C.) with the following history:—

On about the 27th March, 1932, the sight of her right eye began to go dim and three days later her left eye began to go dim also.

When first seen, on 6th April, her sight was: Right eye = 6/36 and Left eye = No perception of light.

Both pupils semidilated: Right pupil contracted to light but did not remain contracted. There was also a consensual contraction of left pupil and it also was not maintained.

The left pupil was quite inactive to direct light and there was no consensual reaction. The ophthalmoscope showed a typical papilloedema of both discs. A swelling of between $1\frac{1}{2}$ to 2 dioptries in each. No hæmorrhages or exudates. Apart from her very natural mental distress she was not ill.

She was admitted to the Rangoon General Hospital, and the first physician was asked to examine her with the object of finding a cause for the condition. His results were uniformly negative. Her other cranial

nerves were normal. She was put on mercury, potassium iodide and strychnine injections.

Towards the end of the second week of her stay in hospital she said the sight of her left eye was coming back. One was doubtful of this till it was noticed that the pupil of that eye was beginning to react to direct light.

From this time onwards the improvement in her sight in each eye continued and she was discharged at the end of two months with full vision (6/5) and full fields in her right eye. Her left eye was the same except that she complained of a faint 'shimmering haze' in front of this eye. This was due to a small centro-caecal scotoma which shows up on a Bjerrum's screen with a 2 mm. test object (white) at one metre. Her distant vision in this eye was '6/5 three letters' and she read Jaeger No. 1 correctly but much more slowly than she did with her right eye.

Up to this time we were unable to find any cause for the condition and were quite in the dark as to the ætiology. The mercury treatment was stopped after a week as her Wassermann reaction was negative.

Some weeks after her discharge from hospital it was discovered by mere chance that she had recently undergone a course of antirabic treatment at the Pasteur Institute, Rangoon, and that her sight became affected about five or six days after her last antirabic injection. She had not connected her eye trouble with the antirabic inoculations and had therefore not reported it to the Pasteur Institute, nor mentioned the inoculations at the hospital.

DETAILS OF ANTIRABIC TREATMENT

The patient, a healthy, normal woman, was bitten by a dog, which was certified rabid, on 3rd March, 1932. She reported at the Pasteur Institute, Rangoon, on 5th March, two days after the injury.

There was one deep bite on the arm, inflicted through the bare skin; the wound had been cauterized with pure carbolic acid.

She was given Class III treatment, i.e., 5 c.c.m. of a 5 per cent carbolized sheep vaccine, daily for 14 days, receiving in all 3.5 grammes killed sheep fixed virus. She attended regularly from 5th March for her treatment, which was completed on 18th March, 1932.

No untoward symptoms whatever were observed during the course of treatment.

A few days ago (4th April, 1933) her eyes were examined again, that is, just over one year since the disease started. Except for the small scotoma her eyes are normal. There is no peripheral contraction of the fields. Her optic discs are of a healthy pink colour; edges distinct; good physiological cups with cribriform plate well shown at the bottom of them. The blood vessels are normal. At no time were there any exudates or hæmorrhages. The latter were looked for even with a red-free light. Right vision = 6/5 and J 1; left vision = 6/5 three letters and J 1 slowly but accurately.

DISCUSSION

The question as to whether this case is an example of the so-called 'post-inoculation paralysis' is a very interesting one. As is well known, antirabic inoculation is occasionally followed by disorders of the nervous system which, though their ætiology is still undetermined, have undoubtedly a causal connection with the inoculation.

These nervous disorders present a great diversity of form, varying from slight weakness of one or both legs, or simple facial paralysis in the mildest cases, through a more severe condition with complete paraplegia, to a very grave and usually fatal ascending paralysis of the Landry type.

Such are the forms in which these disorders are usually manifested, but affections of almost every part of the nervous system, including the various cranial nerves, have been reported.

A careful search of all available literature has failed to bring to light any case similar to this one, in which the part of the nervous system affected was the optic nerves themselves, but there seems no reason to suppose that this part of the nervous system should necessarily be exempt from attack by a disease whose incidence on that system is so widespread.

In a personal communication to one of us, Lieutenant-Colonel H. E. Shortt, I.M.S., Director, Pasteur Institute of India, Kasauli, states that he recollected seeing a report in which optic neuritis, or at any rate blindness, had been observed in animals after antirabic treatment; but he, too, was unable to find the actual reference.

The following points are in favour of this case being one of post-inoculation paralysis.

First, the fact that no other cause for the condition could be discovered, at a time when nothing was known as to her previous antirabic treatment.

Secondly, the incubation period—about 20 days from the first treatment—corresponds with that observed in cases of post-inoculation paralysis, practically all, if not all, of which occur within the first thirty days, reckoning from the date of the first treatment.

Thirdly, her remarkably complete recovery from such a severe condition. Except in the gravest cases and those of the Landry type, the prognosis of post-inoculation paralysis is good, and the tendency is to complete recovery after a longer or shorter period. In this case, serious as the damage appeared to be, both eyes had returned practically to normal in little more than two months.

A PEDUNCULATE LIPOMA

By B. U. PUROHIT, L.C.P. & S. (Bom.)

Assistant Medical Officer, Goodfellow Hospital, Palanpur (N. G.)

THE patient, a Hindu male aged about fifty, came to hospital to seek relief from a large ulcerating tumour in the right gluteal region.

History.—The tumour was first noticed in 1901 as a soft cushion-like pad causing no pain or inconvenience in its early stages. It gradually increased in size until it reached its present dimensions (*see illustration*). It will be noted that it is pedunculated. During the last three or four years it has practically prevented his walking and more recently it has become ulcerated; this induced the patient to come to hospital.

Under infiltration anesthesia with percaïn and adrenalin the tumour was successfully removed.



It was found to be a multi-lobular lipoma with no secondary changes, and it weighed thirty-seven ounces. The case is of interest on account of the unusual size of the tumour and its long pedicle.

AN IRON RING ON THE PENIS

By S. N. CHATTERJEE, L.M.S.*

Palganj Dispensary, Hazaribagh District

A boy, aged about 18 years, was brought to me with the following history:—

To relieve a pain in the penis he placed thereon an iron ring about three-quarters of an inch in diameter and three-quarters of an inch in breadth, which he pushed right down to the base of the organ.

I saw him some hours later and the penis was intensely swollen being about eight inches in length and four and a half inches in circumference; he had complete retention of urine for the relief of which it was not possible to pass a catheter. Eventually after cautiously cutting through the ring with a blacksmith's saw, which operation took about three hours, I was able to expand the ring and remove it, and the patient experienced instant relief.

* Rearranged by Editor.

Indian Medical Gazette

AUGUST

THE CENSUS AND THE MEDICAL PROFESSION IN BENGAL

UNEMPLOYMENT in every walk of life and in every part of the world has been a problem ever since the termination of the great war, and during the last few years of world-wide depression the seriousness of this problem has been markedly aggravated. In India the ryot, even if he has temporarily abandoned his village and sought employment in the town, can return to his home, take up his share in the work of cultivation of the land, and thereby ensure his modest daily requirements. In the Bengal village at any rate actual starvation is almost unknown and, though undernourishment is the rule, it is the nature of the food rather than the quantity that is at fault, so that amongst this class the unemployment problem is not so real. But with the educated classes the state of affairs is very different. Naturally after spending money on education they are not prepared to return to the village and do work which they have learnt to consider the duty of menials, consequently in Bengal, and in many other parts of India, the proportion of this class on the unemployed list is enormous; one has only to advertise for a clerk on Rs. 50 a month to get two or three hundred applicants. The 'learned' professions have suffered with the rest and nowhere is this state of overcrowding more apparent than in the medical profession in the large cities in India.

The population of Bengal in 1921 was 44,599,233, whereas in 1931 there were 51,087,338 persons in the province; this means that during the last intercensal decade there has been a 7.3 per cent increase in the general population. In the 1921 census, the medical profession—including registered and unregistered practitioners and dentists—totalled 43,172, and in 1931 the same group contained 53,424 persons—an increase of 23.7 per cent. Thus the percentage increase in the medical profession is three times that of the increase in the total population, or in other words during this ten-year period the number of individuals per practitioner has fallen from 1,102.5 in 1921 to 956 in 1931.

The census returns for the British Isles for 1931 are not yet available, so for purposes of comparison we will use the figures for the 1921 census of England and Wales; at this time there were 1,564 individuals per practitioner in these two sections of the British Isles. It is true that the English figures do not include unregistered practitioners, whereas those of

Bengal do, but the number of such persons engaged in whole-time work in England is so small that their influence on the total would probably be unappreciable. In Bengal, however, 42 per cent of the persons engaged in whole-time work connected with the healing art are unregistered; nevertheless, they must be included in the calculations, because the influence of these unregistered practitioners on the earnings of the registered practitioners is very considerable, and is often a cause of complaint from the latter. If we exclude the unregistered class, the number of persons in the province per registered practitioner is 1,649.*

For many years the cry in Bengal has been for more medical men for the country districts and to meet this demand small medical schools have been opened in the division-headquarters towns in the province. The position has now been reached when on paper there is an adequate supply of medical men for the whole population, but the fact still remains that in practically every country district in Bengal the provision of medical personnel for the population is far below the ideal. What is the explanation for this anomalous state of affairs, unemployment amongst the medical profession on the one hand and insufficient medical attention for the majority of the population on the other? One of the obvious causes is uneven distribution of medical men in the province.

There is a tendency in Bengal just as in other provinces and other countries for medical men to gravitate to the large population centres. It is not difficult to see the reason for this. The student sees that in the town where he has been educated there are opportunities for a higher grade of practice which his training had taught him to appreciate; he realizes that those pleasant aids to diagnosis, such as x-rays and even the microscope, will probably be for ever out of his reach in a country practice; if he is ambitious he also sees that it is only in the towns that big reputations—and incidentally big fortunes—are to be made; and even if he has few ambitions and is prepared to face

*Since writing this we have received the Bengal Annual Medical List for 1933; this list contains 8,889 names of which 540 have been added, or restored, during the year 1932. There may be a certain number of practitioners registered in other provinces who, though practising in Bengal, have not registered; on the other hand in view of the fact that in the present list we recognize the names of many who have long since left Bengal, and some who have left this world altogether, and that during the year no names were removed 'on evidence of death', the figure is likely to be greater, and not less, than the number of registered practitioners actually practising in the province at the beginning of the year. The discrepancy is hard to explain except on the grounds that the census figures are wrong; in addition to the 42 per cent who admit to being unregistered, there must be another 42 per cent or so who, though unregistered, are posing as registered practitioners. If this is the case our argument regarding the plentiful supply of registered practitioners is weakened but that regarding the bad distribution of the profession in Bengal is strengthened considerably.

medical practice in its simplest form and to treat his patients symptomatically and empirically, he is still faced with the problem of earning his living, which, if he is prepared to bury himself in a country district, where his services are really needed, he may have considerable difficulty in doing. This tendency on the part of the medical profession to congregate in large towns is thus governed by either laudable ambitions or sound common sense; the young doctor feels that it is better to risk starvation in the town than to court it with certainty in the country; one could not, even if one wished, legislate against ambition; the only alternative is to make it worth the while of the medical man to settle in the country. This is a problem which we do not propose to discuss here as it would lead into too many by-paths, as for example into the question of subsidies, and the limitation of the activities of unqualified practitioners, many of whom are uneducated, have a lower standard of living and are governed by no ethical rules, and are a continual thorn in the side of the registered practitioner, especially in country districts, but its solution is one of the most urgent medical needs of the present day.

Another aspect of the problem is also brought out in the recent census. Amongst what might be termed the accessory services to the medical profession (nurses, dispensers, hospital orderlies, masseurs, etc.) the numbers in Bengal have only increased from 14,066 in 1921 to 14,339 in 1932, that is to say by only 1.9 per cent. These figures show that for every 3.7 practitioners in Bengal only one of the assistant group is available.

Though the medical man is taught the rudiments of dispensing and though his knowledge of the action of drugs should ensure that he does not poison his patients, he has not been trained to be an expert dispenser, and if circumstances make it necessary for him to dispense his own prescriptions he will do it less expertly and much more slowly than the trained dispenser. The same is true of nursing; few doctors, even women doctors, make good nurses, and therefore when they are compelled to do work which is really that of a nurse, they are not only wasting their time but they are failing to give the patient the most expert assistance. Thus, this shortage of trained nurses and dispensers, to take the two most important members of this 'accessory' class, is a very serious handicap to the medical profession in this country—it is a state of affairs that exists not only in Bengal but everywhere in India—and it must lead to a very serious waste of time of the practitioner in doing things for which he has not been trained and which could be done by less-expensively-educated persons; as a consequence both the quality and the quantity of his legitimate work will naturally suffer.

In England and Wales a very different state of affairs exists; the 1921 census shows that

for each medical practitioner there were just over five of the assistant class, a complete reversal of the proportions. The great majority of these consists of female nurses. In India women have not yet taken up nursing in the way they have done in England and other western countries, but there is no reason why this gap should not be filled meanwhile, to a much greater extent than it is at present, by male nurses or dressers.

There are thus two lessons to be learned from a study of the census report with regard to the provision of medical relief for the people of Bengal, namely that it is not more medical men but a better distribution of the present members of the profession that is required, and that the value of the work of the qualified doctor could be very considerably enhanced if more trained members of the 'accessory' services were available.

These observations were called forth by a study of the *Bengal* census report; in many parts of India there is a real shortage of medical men per head of population, but the remarks regarding the shortage amongst the accessory services will hold good throughout the whole of the peninsula.

Special Article

A NOTE ON PROFESSOR NICOLLE'S VIEWS ON THE TYPHUS AND RELAPSING FEVERS

By SIR JOHN MEGAW, K.C.I.E.

MAJOR-GENERAL, I.M.S.

Director-General, Indian Medical Service, New Delhi

PROFESSOR CHARLES NICOLLE has an interesting note in the *Bulletin de l'Institut Pasteur* of October 1932 on the differential diagnosis of the various forms of typhus fevers which are of interest to the French doctors in Europe, Africa and the Middle East. He leaves out of account the Rocky Mountain and Japanese River fevers which do not occur in Europe and Africa and apart from them he recognizes three types of typhus, (1) *old-world typhus* conveyed by lice, (2) *benign typhus* conveyed by fleas, and (3) *fièvre boutonneuse of Tunis* or *macular fever* conveyed by ticks.

Typical cases of these forms of the diseases can be distinguished with ease, but there is no diagnostic feature which is of universal application. In old-world typhus the severity, the scantiness of the rash, the prolonged convalescence and the epidemic nature of the disease are usual features. Benign typhus is usually mild and endemic while the tick-borne macular fever is always endemic. From the laboratory point of view benign typhus and old-world

typhus have viruses which are mutually protective, whereas neither protects against the macular fever. An essential difference is that lice can be infected by the two former kinds of typhus but not by the virus of macular fever which is conveyed by a tick (*Rhipicephalus sanguineus*). The Weil-Felix response is also much less pronounced in the case of the macular fever. The rat is readily inoculable with benign typhus and constitutes the animal reservoir of the disease whereas it is practically immune to old-world typhus whose reservoir is the human being.

Nicolle, therefore, proposes to call these two diseases 'historical typhus' and 'murine typhus'. The virus of each of these two forms of typhus is pathogenic for the louse while that of the tick-borne macular fever is not; but whereas the virus of murine typhus is rapidly lethal to lice, some of them dying as early as

The confusion in nomenclature of the fevers of the typhus group is not likely to be lessened by the new proposal of Nicolle. My suggestion to employ the name of the insect vector has obvious practical advantages; difficulty only arises when there is no evidence as to which vector is concerned and in this case we have to fall back on the term 'typhus group fever of unknown vector'. Nicolle's suggestion to employ the name of the animal which is the reservoir of the disease is quite logical, provided that there is only one animal concerned in connection with each fever and also that we know which animal is responsible. Now that the flea has been definitely incriminated as the vector of one kind of fever of the typhus group in some French ports and in the eastern Mediterranean, it is necessary to extend my former classification, based on insect vectors, as follows:—

Fevers of the typhus group

	Louse typhus	Tick typhus	Mite typhus	Flea typhus	Typhus of unknown vector
Synonyms	(Typhus fever, classical typhus, historical typhus, etc.).	(Rocky Mountain fever, Indian tick typhus, fièvre boutonneuse, etc.).	(Tsumugamushi, Japanese River fever, etc.).	(Benign typhus, murine typhus, etc.).	

the third day, the virus of historical typhus is much less lethal to these insects. According to Nicolle this difference shows that the adaptation of murine typhus to lice is of more recent date than that of historical typhus, and on the other hand neither of these two viruses is lethal to fleas although both of them infect these insects and the infection persists for a long time.

This note of Nicolle is of special interest to workers in India. It may be pointed out that the tick-borne macular fever corresponds very closely in all essential points with the disease to which the writer has given the provisional name of *tick typhus*, and it is probably the same disease.

Of the other classifications which have been suggested the best is probably 'epidemic typhus' and 'endemic typhus' but as both tick typhus and mite typhus are endemic and as louse typhus is not always epidemic this classification has serious shortcomings. In fact it is a case of choosing between provisional classifications rather than of suggesting one which has a permanent scientific basis. So far as India is concerned the only vectors regarding which there is clear evidence are lice and ticks, but it is necessary to keep an open mind as to the possibility of mites, fleas or other vectors being concerned in the conveyance of fevers of the typhus group in India.

Summary of laboratory diagnostic features according to Nicolle

	Old-world typhus. (Louse typhus)	Benign typhus. (Flea typhus)	Fièvre boutonneuse of Tunis or macular fever. (Tick typhus)
Insect vector	Louse	Flea	Tick
Epidemicity	Usually epidemic	Usually endemic	Always endemic.
Specificity of virus	Protects against benign typhus but not against macular fever.	Protects against old-world typhus but not against macular fever.	Does not protect against the other two.
Infectivity to lice	Infective	Infective	Non-infective.
Lethality to lice	Moderately lethal	Highly lethal	Non-lethal.
Weil-Felix reaction	Strongly positive	Strongly positive	Variably positive, often negative.
Infectivity to fleas	Infective	Infective	Non-infective.
Rat inoculability	Slight	Pronounced	Doubtful, usually negative.

Relapsing fever group

Nicolle discusses the origin of the virus of the two chief forms of relapsing fever. One of these he calls *world-wide relapsing fever* and the other *tick relapsing fever*. There are a great many types of tick relapsing fever and Nicolle confines himself to the type which occurs in North Africa which is conveyed by *Ornithodoros erraticus*. He deals with the clinical differences between louse relapsing fever and tick relapsing fever and points out that the number of spirochaetes in the blood is very much greater in

louse relapsing fever than in the form which is carried by ticks. The animal *par excellence* which can be used to distinguish the two forms is the guinea-pig; this animal is refractory to the virus of louse relapsing fever, whereas it responds readily to inoculation by the virus of tick relapsing fever, which causes a pronounced attack of the disease with relapses accompanied by the presence of numerous spirochaetes in the blood. Here again the provisional classification into 'tick relapsing fever' and 'louse relapsing fever' appears to be the most convenient.

Medical News

D.P.H. COURSE AT THE ALL-INDIA INSTITUTE OF HYGIENE AND PUBLIC HEALTH, CALCUTTA

The courses of instruction for the D.P.H. examination will commence from the 15th October, 1933, at the above Institute, in collaboration with the School of Tropical Medicine, Calcutta.

Applications for admission should be made by the 31st August next, to the Director, All-India Institute of Hygiene and Public Health, 21, Central Avenue, Calcutta.

'MEDICAL PRESS AND CIRCULAR'

THERE are very few numbers of this *Gazette* in which there is no extract from the *Medical Press and Circular* in the Current Topics section, so that our readers scarcely require an introduction to this essentially practitioners' journal. It is a weekly publication, and it must be a very rare occurrence for a practitioner not to find something in the number that is of immediate practical importance to him. The policy of the journal is conservative in that they do not allow writers with newly-discovered but ill-tested forms of treatment to contribute, but when any new discovery is established the editors always manage to get an article from some sound authority on the subject. Dr. Harry Campbell who has been editor for a number of years has just retired and though we miss his genial editorial notes—especially his weekly attack on the rash motor-car driver—we see no signs of any alteration in policy or any falling off in the interest of the editorial commentaries.

At the beginning of this year this journal commenced to issue a series of quarterly supplements; each is to be on some subject of special interest to the general practitioner. The last of these supplements is on common skin diseases; one of the articles has been extracted for our Current Topics section and will appear in our next number. The supplement is printed on special art paper, and the illustrations are numerous and well reproduced. The whole will form a very useful addition to the practitioner's library, as these supplements are certainly worth keeping and binding.

BENGAL COUNCIL OF MEDICAL REGISTRATION

The following extracts are taken from the minutes of the meeting of the Bengal Council of Medical Registration held on 8th February, 1933, forwarded to us by the Registrar under letter dated 28th June, 1933:—

The government resolution on the appointment of Dr. B. N. Ghosh, L.M.S., F.R.F.P. & S., L.M., and Dr. T. Ahmed, M.A., D.O.M.S., F.R.C.S., representatives of the Bengal Council of Medical Registration and the Governing Body of the State Medical Faculty of Bengal, as

members of the Bengal Sanitary Board for one year with effect from 22nd December, 1932, was recorded.

The government notification regarding election of Major B. H. Singh, I.M.S., in place of Dr. K. M. Basu under clause (c) of section 4 of the Bengal Medical Act, 1914, was recorded.

Government expressed their inability to accede to the recommendation of this Council that medical certificates granted by registered medical practitioners to gazetted officers applying for leave be accepted and it was decided that government be requested to reconsider their decision.

On an application from the registrar, Rangoon University, it was decided that a report be made to the local government under section 18 recommending that the M.B., B.S. degree of the Rangoon University be recognized as registrable in Bengal.

Reports on the inspection of the undermentioned medical schools were considered:—Calcutta Medical School, National Medical Institute, Jackson Medical School, Jalpaiguri, and Chittagong Medical School. It was decided to recognize the Chittagong Medical School and to recognize temporarily for one year the Jackson Medical School, as institutions qualified to train and send up candidates for the Licentiate Examination up to the Final standard.

The following gentlemen were appointed members of a Standing Committee to inspect medical schools:—

Lieut.-Col. A. D. Stewart, M.B., Ch.B., D.P.H., I.M.S.

Sir Kedarnath Das, Kt., C.I.E., M.D.

Dr. S. K. Mukherjee, D.O., D.O.M.S., F.R.C.S.

Mr. Mrigendralal Mitra, F.R.C.S.

Dr. A. D. Mukherjee, L.M.F.

On the motion of Dr. S. C. Sen Gupta, M.B., Ch.B., F.R.C.S., M.D., it was decided that the schools be allowed to take in 10 per cent in excess of the normal permissible number of admissions in the first year class.

The undermentioned gentlemen were appointed members of the Penal and Ethical Cases Committee for the year 1933:—

Sir Kedarnath Das, Kt., C.I.E., M.D.

Lieut.-Col. T. C. Boyd, F.R.C.S., D.P.H., I.M.S.

Dr. J. N. Maitra, M.B.

Dr. Pramathanath Nandi, M.D.

Dr. A. D. Mukherjee, L.M.F.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of August 1883, Vol. XVIII, pp. 209, 210, 211, 225, 226 and 227)

On the radical cure of hernia by Spanton's method

By ARTHUR NEVE, L.R.C.P. & S. (Edin.)

Mission Hospital, Kashmir

A CASUAL glance through recent medical literature shows the attention which is being devoted to the subject of hernia. It is only within the last few years that

the radical cure of hernia has come within the range of practical surgery. In this country, where there is difficulty in obtaining suitable appliances, and where surgical help is not always immediately available, a radical cure becomes of primary importance. In England it will likely long remain the rule that only cases in which a truss does not yield efficient support, or those liable to recurrent attacks of strangulation, will be submitted to operative measures. But in India, if it be possible to operate without danger and with fair chance of success, it is desirable to do so in almost every case that presents itself.

What are the forms from which we have to select? 'The older methods were', I quote from Birkett, 'castration; cauterization of the orifice and neck of the sac; ligature applied round the neck; incision of the sac and subsequent healing of the wound by granulation; excision, suture and scarification of the sac; detachment of the sac from its connections and returning it into the abdomen; immediate and forcible compression of the sac by a bandage or truss, cold douche; stimulating injections, especially tincture of iodine'.

The methods were barbarous. They were all faulty in conception and futile in practice; often, too, highly dangerous. None of them were aimed at the real seat of the disease—the patent inguinal canal.

But my own experience during the past year with Spanton's screw points to a method as safe as it is simple, and affording good results.

Nine cases have been thus operated upon; in most cases the patient was as soon as seen put upon the table, and having been anesthetized, the instrument was introduced.

I never use the spray while thus operating. The performance of the operation, including the incision of the skin, partial separation of the sac, introduction of the indicating finger, and insertion of the screw, scarcely occupies two minutes.

The ring usually admits of two points on either side being approximated, by two complete turns of the instrument. As this is done the pillars are felt not merely to be brought in contact but to be rolled over one another and the finger is squeezed out of the canal. One or two more turns of the screw being given, the point of the instrument is brought out of the scrotal wound. In all these steps Mr. Spanton's instructions are closely followed. A strip of lint soaked in carbolic oil is wound round the ends of the instrument: this is the only dressing.

By the third day there is always some hardness and swelling over the track of the screw and a few drops of pus exude. The instrument is left *in situ* till usually the seventh day, sometimes longer. At this time it can be withdrawn with ease and with little pain.

The wounds are then suitably dressed, and for a few days discharge a few drops of pus; but the sinus quickly heals, sometimes in five or six days. The swelling gradually lessens, but the hardness remains and conveys an impression of great security.

Medical women for India

The movement, which we discussed at some length in our issue for July 1882, has assumed a practical shape, and is about to enter upon the phase of experiment. The somewhat visionary proposal to organize a medical service of lady doctors to meet a demand which has not been shown to exist, and fulfil a purpose the reality and success of which are doubtful, has been laid aside and wiser and more moderate counsels now prevail. It is unfortunate that philanthropy is so often associated with want of common

sense, and the divorce between these attributes has been very manifest in much that has been written on this subject. Arithmetic is often made to supply the place of investigation in India, and it has been caused to do duty in this question in the following fashion. The population of India is 250 millions, the female population must therefore be over 100 millions. Allow a lady doctor to every 100,000—a very moderate proportion—and the number required for India would be 1,000 at the very least.

This was the view which a majority of the Council of the Calcutta Medical College took when the question of the medical education of Indian females was recently referred to them. They considered that the requirements of the country pointed rather to the provision of educated midwives and nurses than of full-blown lady doctors, that these requirements were being very imperfectly fulfilled, and that the social experiment (for even in Europe and America the matter is still in an experimental stage), of educating women for the medical profession would be more safely conducted by gradually developing existing arrangements, of whose necessity and propriety there cannot exist a doubt, than by proceeding *per saltum* to the extreme phase of the undertaking. The Government of Bengal has, however, assumed the responsibility of throwing open the Medical College and hospital to females, and one young lady, a B.A. of the Calcutta University, has availed herself of the privilege, and is now enrolled as a regular student of the College, and diligently attending lectures and pursuing her studies. In Madras, at the instigation of Surgeon-General E. Balfour, lady students were admitted in 1875 into the Medical College under special rules.

Current Topics

Commercial Aspects of Bacteriophage Therapy

(From the *Journal of the American Medical Association*, 20th May, 1933, Vol. C, No. 20, p. 1603)

THE premature commercial exploitation of 'bacteriophage' has no doubt induced expenditure of considerable sums for therapeutically inert preparations of bacteriophage-lysed bacterial filtrates. Laboratory scientists suggested the subtle and misleading name 'bacteriophage'. True, certain bacterial filtrates introduced into a limited volume of fluid culture medium will in many cases cause the suspended bacteria to die. The dead bacteria disintegrate. After disintegration, a hundred times the original lytic titre is demonstrable in the culture medium, together with numerous other autolytic products.

Ignoring possible enzymes, hormones, genes and other growth factors, imagination pictured this lysis as the result of a hypothetical bacteria-digesting virus. A specifically active lytic agent of this character would logically not affect other factors in the animal body. It was argued that it might penetrate to the remotest corner of infected tissues in search of its specific diet. The well-known fact that test-tube lysis does not take place in the presence of gelatin, egg white or numerous other colloids was disregarded. The well-confirmed evidence that similar inactivations take place in the presence of mucus, fibrin, pus, blood serum, erythrocytes, fixed tissue cells and certain urinary crystalloids was also ignored by commercial interests, in spite of the fact that voluminous data have been published during the last twelve years.

The commercially-promoted reading matter also carefully evaded references to the well-confirmed evidence that limitation of volume is a necessary factor in test-tube lysis. In other words, 'bacteriophage' has

no appreciable injurious effects on homologous bacteria until the extrabacterial concentration of bacteriophage is raised to a certain critical level. Publication of this fact might have suggested to prospective purchasers that the necessary critical concentration could rarely be reached or maintained in any tissue supplied with a capillary circulation, or in any urinary or cerebro-spinal space with its constant lavage with new fluid.

Under the numerous test-tube conditions in which lysis does not occur, 'mutation' or 'adaptations' of the exposed bacteria take place, with the production of bacteriophage-resistant strains. These strains cannot be lysed even under most favourable test-tube conditions. The commercial literature failed to announce that 90 per cent of all typhoid bacilli freshly isolated from typhoid stool or typhoid blood are bacteriophage-insusceptible variants. One also seeks in vain for any reference to bacteriophage anaphylaxis or to anti-therapeutic 'negative phases', the well-known dangers and contraindications with certain other protein mixtures or bacterial vaccines.

Competent investigators who have made impartial and conscientious efforts to determine the clinical value, limitations and dangers of the Twort transmissible lysin marvel at the policy of suppression of scientific fact in the promotion of bacteriophage preparations. If data suggesting limitations and dangers had been suitably set forth in advertising prospectuses, clinical trials might have been limited to certain well-defined pathologic conditions leading eventually to official endorsement, whereas the Council on Pharmacy and Chemistry has not yet accepted such preparations. Moreover, there is a rapidly growing resentment and distrust of the whole bacteriophage promotion, which certainly will delay final clinical evaluation.

Premature exploitation of the Twort lysin is by no means an isolated example of this short-sighted policy. The opsonic index was successfully sold to the medical profession, long before its technical errors were assayed, before any critical test was made of the assumed quantitative parallelism between specific opsonic index and specific immunity. Perhaps a million doses of leukocytic extract were injected before any quantitative tests were attempted to prove that such injection causes anything more than a borderline reaction of negligible therapeutic value. 'Anti-cold vaccines' were widely sold commercially and even yet the ætiologic factor of common colds is unknown and the evidence of usefulness doubtful. The Council on Pharmacy and Chemistry is a safe guide to follow at a time when all sorts of untried therapeutic plausibilities are being launched on the medical profession.

Acne Rosacea

By SAMUEL AYRES, JR., M.D.

and

NELSON PAUL ANDERSON, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. C, 4th March, 1933, p. 645)

SINCE our recognition several years ago of the presence of *Demodex folliculorum* in the majority of our patients with acne rosacea and an allied condition which we have designated as pityriasis folliculorum (*Demodex*), our therapeutic results have been far superior to those obtained by the usual treatment of acne rosacea.

In view of the fact that Kaufmann-Wolf called attention to the frequent occurrence of *Demodex folliculorum* in the pustules of acne rosacea as long ago as 1925, it seems rather surprising that so little recognition has been accorded this valuable contribution. One might argue that, because *Demodex* is a more or less 'normal' inhabitant of the human skin, it is without ætiologic significance. Granting that the organism may be found on apparently normal skins, it usually is present in small numbers and may be found only by

expressing sebum from some of the oil glands by pressure. This is in striking contrast with the large numbers of *Demodex* that can easily be found in many cases of acne rosacea; it is not uncommon to find ten or fifteen organisms in a single tiny follicular scale or superficial pustule. It would be just as fallacious to say that, because the staphylococcus is found on many healthy skins, it is without any causal relation to furuncles or carbuncles.

In two previous communications we have called attention to the frequent occurrence of *Demodex* in acne rosacea and in pityriasis folliculorum (*Demodex*), a newly described clinical entity which is probably closely related to acne rosacea. On the other hand, we have been able to find *Demodex* only rarely in the pustules of acne vulgaris.

Our reasons for regarding *Demodex folliculorum* as an ætiologic factor of importance in these two disorders are as follows:

(1) The organism is easily found in from moderate to large numbers in pus from superficial lesions or in the dry follicular scales, whereas it is usually absent in acne vulgaris.

(2) A rapid clinical improvement or cure follows the application of strong anti-parasitic applications and the daily use of soap and water.

(3) Accompanying the clinical improvement there is a corresponding decrease in the number of *Demodex folliculorum* organisms that can be isolated from the skin.

Since the publication of these earlier reports, a total of seventy-seven patients in private practice have been seen who have presented the clinical picture of acne rosacea or pityriasis folliculorum (*Demodex*). The same conclusions that have been mentioned are applicable to this larger series. Of these patients, fifty presented typical cases of acne rosacea. During the same period of time that these cases were collected, only thirteen cases of acne rosacea were seen which failed to reveal *Demodex folliculorum*.

It was noted that a considerable proportion of the patients used soap and water infrequently or not at all. It is felt that the excessive use of cold cream and powder and the substitution of cleansing cream for soap and water favour the development and multiplication of these organisms. This may partially account for the recognized predominance of acne rosacea in women. A small droplet of pus obtained from a superficial pustule the size of a pinhead, placed on a glass slide and macerated with a drop of 40 per cent potassium hydroxide or glycerin, will usually show under the microscope from one to fifteen or more organisms. Usually the contents of two or three pustules are examined, or in those cases in which the complaint only of dry, rough skins is made, some of the minute dry follicular scales are picked off and examined in the same manner.

When such an examination shows the presence of *Demodex folliculorum*, local treatment alone will usually effect an improvement that is almost unparalleled in dermatologic therapy. Until recently we have employed an ointment such as is used for the treatment of scabies; betanaphthol, 2 gms.; sublimed sulphur, 4 gms.; balsam of Peru, 15 gms.; petrolatum, 15 gms. In spite of the fact that many of these patients have declared that their skin was so delicate that they could not even tolerate soap and water, we have obtained excellent results usually within from one to three weeks. The patient is instructed to wash thoroughly with soap and water every night and to apply the ointment for only three nights. There is usually a temporary increase of redness with some desquamation immediately following the application of the ointment, which, however, subsides in several days. It is usually necessary to have the patient repeat the ointment once or twice a week for several weeks. There have been but few recurrences in our series of cases, and those which have recurred have been rather mild and have responded promptly to further treatment.

More recently we have used Danish ointment in the same manner with equally good results and with less irritation.

We do not feel that the improvement is due to the effect of sulphur on the seborrhœa, because some of the most striking results occur in those cases presenting dry skins and with no evidence whatever of seborrhœa. The scaling mentioned in cases of pityriasis folliculorum is not of a seborrhœic type but rather consists of fine dry inconspicuous white scales about the mouth of the sebaceous ducts or the base of the lanugo hairs, resembling the frosting resulting from an ethyl chloride spraying. Microscopic examinations of the contents of pustules or scales made on each visit show a progressive diminution in the number of parasites until no more pustules or scales are available, which often occurs after the second or third week.

Of course, those patients who do not show *Demodex* must be treated according to the local and systemic indications in each case and undoubtedly a few of the cases with *Demodex* infection may need supplementary treatment, directed to the nervous system, gastrointestinal tract, and so on.

Summary and conclusions

(1) In seventy-seven cases of acne rosacea and pityriasis folliculorum (*Demodex*), *Demodex folliculorum* was found in superficial pustules and follicular scales in from moderate to large numbers.

(2) In sixty-nine of these patients whose results could be followed, striking clinical improvement or cure was obtained in all but three cases by the use of a strong antiparasitic ointment.

(3) Out of sixty-three cases of typical acne rosacea seen during the past two years, in which examination for *Demodex folliculorum* was made, the organism was found in fifty cases. With the exception of three patients who did not return for observation, excellent results were obtained in all but two of these cases by the use of a strong antiparasitic ointment without any other treatment.

(4) Irrespective of any argument concerning the causal relationship of *Demodex folliculorum* to acne rosacea, the fact remains that local antiparasitic treatment as described has given clinical results far surpassing anything in our experience with this disease.

Some Common Skin Affections of the Tropics and their Treatment

By W. E. COOKE, D.P.H.

and

HUGH WILLOUGHBY, D.T.M. & H.

(Abstracted from the *Journal of the Royal Naval Medical Service*, Vol. XIX, January 1933, p. 14)

THERE are many common skin conditions met with in those who serve or have served in the tropics which are easily recognized. We have selected some of the commoner skin diseases which pass through our skin department and quote the treatments which we have found successful.

Hyperidrosis.—General sweating, being usually dependent on some systemic disease, is of less concern dermatologically than localized sweating. The latter type has certain varieties, either neuritic in origin, where the skin area supplied by a particular nerve perspires freely, or due to hyperactivity of the sweat glands, especially in parts well heated by clothing or subject to 'folding', as in the case of the groins.

Anæmia, debility and alcohol are, of course, predisposing causes.

Treatment.—This depends entirely at what stage of the disease one is consulted in the matter. General health must first receive attention. Increase of tone in the muscles, as pointed out by Unna, should be a basis on which to begin: this can be accomplished by periodic stimulation, friction, etc.

The axillary and femoral areas are best tackled by means of (a) absolute cleanliness by frequent washing and (b) astringent applications followed by dusting powders. Formalin, one teaspoonful to a pint of water, is both cheap and efficient, and after dabbing on the affected area should be allowed to dry and not towelled. If the palms and soles are chiefly at fault it is important to recognize whether it is a 'hot sweat' or a 'cold sweat'. If hot, then wash the parts with weak borax solution, if cold bathe in hot water first, carefully dry the parts and apply

Rx		
Ichthyole	..	āā 5i
Olei terebinthe	..	5ss
Camphoræ	..	ad 5i
Unguentum zinci oxidi	..	

Local treatment must first be given by emollients and soothing ointments in cases where decomposition has given rise to dermatitis. Hebra's ointment (Emplastum plumbi cum vaseline) applied on lint is valuable.

Chromidrosis needs no special description and is often met with. Unfortunately, treatment is not very satisfactory, but scrupulous cleanliness and sponging, morning and night, with 1 : 1,000 perchloride spirit will do much to relieve the condition.

Urticaria.—The causation of this condition is threefold:—

(1) External irritants—stinging nettles, flea-bites and many other animal and vegetable substances used in washing, dyeing and cleaning clothes, etc., which may be classed as chemical irritants.

(2) Internal irritants—poisons conveyed to the skin by the blood-stream, such as drugs, e.g., copaiba, and foods, e.g., lobster, mushrooms, strawberries, etc.

(3) Reflex irritants—primarily intestinal helminthic infections or uterine and ovarian diseases. It is worth while bearing in mind that anomalous outbreaks of urticaria may often be an indication of liver diseases, such as cirrhosis and gallstones.

Two varieties of urticaria to which special names have been given are lichen urticatus (vel urticaria papulosa) and giant urticaria.

Treatment.—Obviously determination of the cause is the remedy—not always an easy matter. Allergic conditions must be sought for, and in this respect skin tests with various protein substances are useful.

Drug treatment for urticaria is limited, ichthyol given in capsules (adult dose min. v, t.i.d.) being the best. Salicylate of soda is always worth a trial, and purges will be found helpful in all cases.

Scabies.—This infection is too common to need description. Wrong treatment being, in our experience, more common than proper treatment, it is worth describing in some detail. There is a great temptation to overdo the sulphur baths, and the last state of the patient is often thus rendered worse than the first, caused by the infection itself. We recommend the following routine:—

(1) Bathe the patient in hot water containing sulphide of potassium 3 oz. to 30 gallons of water. Allow the patient to soak thoroughly for twenty to thirty minutes, then thoroughly scrub him with a strong nail-brush. (An attendant should do this to ensure thoroughness, and that all parts may be reached.) A further period of ten to fifteen minutes soaking should then be insisted on.

The patient is next rough-towelled and rubbed all over with sulphur ointment.

(2) While in the bath the patient's clothes should be steam disinfected, and besides clothing all bedding should be similarly treated.

The baths should be given once daily on three successive days, the inunction with sulphur ointment twice on the first day and once after bathing on the second and third days.

Disinfection of clothes and bedding should be done daily for three days.

Any further irritation after this treatment is due to sulphur ointment and not to scabies. Discontinuance of the ointment will cure this.

Furunculosis.—This is usually a staphylococcal infection of the hair follicles or sebaceous glands. Any condition causing debility and so lowering the resistance of the individual is a predisposing factor.

The urine of all patients suffering from furunculosis should be tested for sugar, as a transitory glycosuria occurs in severe cases.

Treatment.—Poulticing and early incision are inadvisable: indeed, incision in certain places such as the nose, upper lip and face generally may be followed by such serious consequences as thrombophlebitis, embolism, cavernous sinus thromboses, meningitis, septicæmia, pyæmia and even death.

Application of Unna's mercury and carbolic plaster gives excellent results. Cleaning with spirit or tincture of iodine and then painting with pure ichthyol and covering with a pledget of cotton-wool is excellent and should be renewed daily.

Application of a proprietary paste called 'Ilon' and deep subcutaneous and intramuscular injections of colossal manganese or manganese butyrate 0.5 to 1 c.c. every four or five days has been found to be very successful in bad cases.

Vaccine therapy (either stock or autogenous vaccines) is in our experience more useful in chronic cases than in the acute condition.

Tinea cruris.—Dhobie itch is so common that a description would be superfluous.

Treatment.—The first thing to be done is to cleanse the affected area thoroughly with soap and water. After so doing a variety of treatments may be tried, all of which are equally successful.

If severely inflamed, preliminary bathing with lotio calaminæ is advisable, or ichthyol, or a 10 per cent solution of sodium hyposulphite may be used.

Any of the following will then be found suitable applications:—

(1) Whitfield's ointment.

R̄ Acidi benzoici	.. }	āā gr. xv
Acidi salicylici	.. }	
Parafini mollis	..	5ii
Coconut oil	ad 5i

(2) Three per cent silver nitrate solution.

(3) R̄ Resorcinol	5i
Acidi salicylici	..	gr. v
Vaseline }	āā 5iv
Lanoline }	

(4) Liniment of iodine may be used on thick-skinned individuals, but is not advised for Europeans.

A dusting powder made of equal parts of boric acid, zinc oxide and starch should be used freely when necessary.

'Hong-Kong foot.'—This is a ringworm which is a very common occurrence abroad and persists in cooler climates unless energetically treated. The causal fungus is an *Epidermophyton*. Occurring as a rule during the summer months it starts as a vesicular eruption on or between the toes or in the hollow of the sole.

Treatment.—(1) Remove the epidermis by soaking well in hot salt water and then apply, night and morning:—

R̄ Acidi benzoici	.. }	āā gr. xv
Acidi salicylici	.. }	
Vaseline	ad 5i

(2) Obstinate cases react to

R̄ Chrysarobini	..	gr. xx
Acidi salicylici	..	gr. v
Vaseline	ad 5i

This ointment stains clothing, etc., and should be rubbed in after washing the feet in soapy water. The feet should afterwards be bandaged.

It is important to change the socks frequently and these should be disinfected before use.

A Simple, Precise Technique for Blood Transfusion

By HAROLD DODD

(Abstracted from the *Practitioner*, Vol. CXXX, No. 3, March 1933, p. 390)

Blood transfusion is probably not used so widely as it deserves. There are three possible reasons for this: (1) The technical procedure of grouping the bloods of the donor and recipient. (2) The impression that special training is necessary to use the fragile and expensive apparatus. (3) The old tradition still lingers, that it is a 'tricky business'.

Thanks to the initiative of the British Red Cross Society, many of our larger towns are provided with an established Transfusion Donor Service, the groups and Wassermann reactions of whose members are already determined. In exceptional urgency in a surgical case, the recipient's group need not be known, and a universal donor (group 4) can be used, after first testing the bloods together. In the absence of an available Donor Service, relatives or friends usually offer, but a donor tested against syphilis and malaria, if available, is preferable as there have been tragic cases of transmission of these diseases, for example, a son has given his father syphilis. Generally, the donor and recipient should be of the same group, and further their corpuscles and serum should always be tested together. The second objection, about the technique and apparatus, is not a real one; familiarity with intravenous therapy is essential, but this is now general as a result of the frequency of varicose vein injection; the apparatus is simple and can easily be improvised. A successful procedure depends on a punctilious attention to details, and this applies particularly to those who do emergency transfusions occasionally, when a simple, reliable method is essential.

The indications.—Between three hundred and five hundred women die annually from post-partum hæmorrhages, some of whom might be saved by a timely transfusion. This valuable help is available to the country practitioner, by ringing up his physician, surgeon or pathologist, all of whom do transfusions, and in a short time a donor or the collected blood is at the patient's bedside.

For instance, recently in the country, a transfusion was urgently needed after a severe post-partum hæmorrhage. The doctor sent a test tube of the patient's blood to a town with a likely donor (her husband). These bloods were matched, found to be compatible, and a pint was citrated and collected in a thermos flask. An hour later, the blood was injected.

This case illustrates the possibilities of the transportation of blood, by car, train or aeroplane. Transfusion is most useful in the emergencies of medicine, i.e., hæmatemesis (even while hæmorrhage is still going on); in surgery, before, during and after operation; and in obstetrical conditions. It is equally effective in adults and children. It renders partial gastrectomy, splenectomy and many other operations possible and safe; in the case of rectal carcinoma, transfusion has reduced the mortality from 20 to between 5 and 10 per cent.

The technique of the transfusion.—To collect blood, citrate it, and inject it, are the essentials of the procedure and surely simple; but every conceivable accident has occurred to make it seem difficult and fraught with pitfalls.

The apparatus.—I have tried several methods and specialized apparatus and experienced numerous mishaps. The following simple, old technique is available or can be improvised from material in doctors' surgeries, chemists' shops and hospitals. It consists of:—(a) Sterile dressings for the patient and donor. (b) A Record syringe 5 or 10 c.cm. for several purposes, but chiefly to act as a handle to insert the needle into the veins. (c) Three new or sharpened Record needles: (1) a fine hypodermic, to inject the local anæsthetic; (2) a large bore needle to withdraw the donor's blood;

when this acts as a control—is administered blood is are pre-blood-p use as prepara flask to boiling, 1 in 46 thermc to the solutio on its thoul blood, lost. here meas and t able pint do as or th piece rubb the Rec intr vein artery forceps.

M.B., F.R.C.S. (Edin).

District Medical Officer.

Dhanbad.

28-3-36.

In a fat or bloodless recipient, the following instruments will expose the vein by cutting: (1) A scalpel or sharp pocket knife, dissecting forceps, aneurysm needle, and a pair of pointed scissors. (2) Ligatures: catgut or thread to tie the vein and suture the skin. (3) A cannula, or the Record serum needle, will be equally efficient and avoid dividing the vein.

The operation.—This resolves itself into three stages: (1) Testing the bloods. (2) Collecting and citrating the blood. (3) Injecting the citrated blood.

Testing the bloods.—This is admirably described in Denis Browne's article, as follows:—

'Pipettes, test tubes, wooden sticks for stirring the blood, Hagedorn needles for pricking the skin, a white glazed tile on which to examine the bloods, a grease pencil for writing on it, a lens to magnify the reaction, a bottle of normal saline and a bottle of spirit. The Moss grouping is a very useful indicator of what the reactions of blood are likely to be, but before transfusion it should be determined what the reaction actually is. For this, about 2 c.cm. of each blood is needed, and in many cases that of the recipient can be obtained from an operation wound, an injury or the placenta. Two drops are picked up with a pipette and blown into 5 c.cm. of saline. The rest is allowed to clot or is centrifuged in order to separate the serum. A drop of each serum is mixed with each opposite solution of corpuscles in a patch of the tile that has been isolated and labelled by the grease pencil. The mixture is then watched for any clumping of the red cells. The dilution of the donor's blood makes the reaction easy to interpret by preventing rouleau formation, and if agglutination occurs (this means incompatibility), it results in a very characteristic "cayenne pepper" appearance of red granules in the clear serum. If possible, twenty minutes should be allowed to elapse before it is decided that the bloods are compatible, but it is usually possible to make out the result in the first five minutes after they are mixed'.

The collection of the blood.—Examine both arms of the donor and select a large vein, the median basilic being the most suitable. In London many donors have several puncture scars, some as many as twenty. It is unnecessary to 'cut down' on a donor's vein to collect blood; donors object to it strongly, and the Transfusion Service forbids it in their members. If the veins are

(they are occasionally in obese or women arm in a dependent position for five water; in addition, put the blood-bag round the arm and pump it up when there is usually no difficulty in the vein. Loosen the donor's neck and he lies on a firm, high table; I prefer the. Before use, rinse everything with solution.

the donor's arm, from the shoulder to the limb can then be handled by the hands, pulse felt, etc.). Inject a c.cm. novocain intradermically over the site. This anæsthetic is not a courtesy to the donor. The large needle can thus be used. Massaging this spot with a sterile cloth to remove any small resulting swelling which might

the anæsthetic is taking effect, fit the large syringe and, with citrate solution, fill it several times, and finally half-fill it. Use the Record needles, take care to cover them with a protector, lint, etc., when they are dropped into the tray dish, the point may be knocked off, it back, thus jeopardizing, before the successful entry into the vein. Repeatedly care due to this unnoticed incident.

the rubber tubing or blood-pressure bag over the selected vein; if tubing is used, tension so as not to affect the strength of the veins are distended by the arterial flow. The blood-pressure apparatus is more accurate and comfortable for the donor and patient alike; I apply it at a pressure of 50 mm. (venous pressure being about 30 mm.).

(4) With the donor's arm out at 45° on an arm rest, the vein is punctured by transfixing both its walls with the needle, the opening facing upwards, then rotate the needle 180° (this is important), thus the opening faces downwards; now, whilst sucking with the syringe, the needle is very slowly withdrawn, until blood appears copiously in the barrel. This method ensures entering the vein; the essential is to introduce the needle firmly enough to pierce cleanly, and not to push the wall of the vein before the point. An alternative method of entering the vein is to puncture it with the needle opening downwards, as in the second stage of the former method. This is advocated by some as being less likely to fail to draw the blood. The ultimate result is the same; it is a matter of personal preference.

When the donor's skin is thick or scarred by previous punctures, entering the vein may be facilitated by making a tiny nick $\frac{1}{2}$ in. long in the skin with a pointed scalpel; thus the needle point can be placed actually on the vein before attempting to enter it. When blood enters the syringe, the assistant places the glass jar (containing the stirrer and 2 oz. of 4 per cent citrate solution) beneath the needle; the syringe is gently detached, and the blood flows briskly into the jar; the arm may need turning slightly. The surgeon steadies the needle throughout the collection period, usually five to ten minutes. The blood is slowly stirred by the assistant or the operator, the jar standing on an adjusted stool. The conventional rubber tubing on the needle to lead the blood into the jar is unnecessary; it adds to the risk of clotting by increasing the foreign surface over which the blood must pass.

(5) The donor is watched and given a warm drink should he feel faint; it is advisable to offer this before the transfusion begins. He takes a bandage in the hand of the arm being used, and squeezes it slowly and firmly 10 to 20 times per minute; this helps the expulsion of the blood—a quick collection minimizes clotting in the needle and cooling. When the amount required is secured, the band round the arm is gently released, the vein is collapsed by a swab placed firmly over it where the needle enters, and the donor's extended arm is carried upwards, when the needle is

withdrawn. A firm dressing is pressed over the puncture, and the elbow (still raised) is firmly bandaged (bandage in donor's hand). Acutely flexing the elbow after removal of the needle and while bandaging encourages hæmatoma formation by obstructing the venous return.

This is elaborate treatment of a needle puncture, but stiffness of the elbow, cellulitis, phlebitis, hæmatomas, small abscesses and axillary adenitis have occurred, causing pain, temporary disability and inconvenience; if care is taken, they never occur. The donor is then given a meal, thus ensuring rest and nourishment after the loss of blood. Donors are instructed to remove the wool of the dressing next day.

Difficulties may arise during the collection. Failure to enter one vein calls for trial of another. The blood may clot in the needle; try passing a stilette, but this is not usually effective, so take the needle out and a brisk stream of blood often follows. By turning the sterilized arm towards the flask this is caught. This vigorous flow often completes the desired quantity; that it has touched the sterilized skin is no bar to its use. The blood is carried to a safe place (accidents have happened through omitting this precaution); to keep it warm it is stood in an enamel jug containing water at 110°F., covered by sterile gauze. A jug is better than a bowl; the jar may topple over in the latter. If a thermos flask is used, the boiled cork is inserted, and the blood is ready for transport.

The injection of the citrated blood.—The patient lies undisturbed in bed. If an assistant is available, whilst the blood is being collected, an intravenous saline to the recipient can be slowly given, thus the blood can be introduced without delay. In an urgent case this intravenous saline can be started before drawing the blood; it may keep the patient alive during a critical 15 minutes, for example in a ruptured spleen or kidney.

The injection should take from 40 to 60 minutes; this slow introduction is vital to the complete success of the transfusion. Any less time risks: (a) collapse, due to heart failure, precipitated by the rapid increase of circulating fluid. This is not unlikely in aged toxic or debilitated patients. As a prophylactic, before the transfusion, give an injection of digitalis gr. 1/100 or diginutin $\frac{1}{2}$ dr. (B. W. & Co.) by mouth. (b) A brisk reaction due to some incompatibility of the bloods and not allowing time for dilution of the 'foreign' serum and corpuscles; this causes tingling pain throughout the body, backache, restlessness, air-hunger, faintness, thirst, sweating, rigors, and occasionally sudden vomiting or call to defæcate; the pulse quickens and the temperature rises. To avoid this, take 10 minutes to inject the first 2 ounces, and carefully observe the patient.

The patient's eyes are lightly covered, and he is moved to the side of the bed where the surgeon proposes to work. A good light is essential. Even in collapsed patients, it is often unnecessary to 'cut down' on the vein. If the limb is hung down and the blood-pressure bag applied to the arm at 50 mm. Hg, the median basilic and median cephalic veins will fill sufficiently for puncture by a sharp, fine serum needle. Prepare the arm and place around it the rubber tubing or blood-pressure bag, tensioned as already mentioned. Take the funnel and tubing, and rinse with normal saline, carefully expelling the air bubbles until the fluid flows through freely, leaving the funnel half full. This ensures that the tubing is patent; occasionally I have found it choked by clots from a previous transfusion. The assistant holds the apparatus, or, if working single-handed, it is suspended from a stand, hook, or bed-rail above the patient's arm. The rubber tubing is occluded by the assistant's fingers, or an artery forcep.

Insertion of the needle into the recipient's vein.—Half-fill the Record syringe with citrate solution, fit the serum needle to it, carefully inspecting its point. Deliberately transfix the vein, rotate the needle, and withdrawing suck with the syringe; blood usually enters, and, if so, proceed carefully as follows: (1) Unclick the

rubber tube round the patient's arm (this permits venous return again). (2) Inject the blood and citrate in the syringe into the vein. By this step the needle is cleared of blood and filled with citrate solution; thus the recipient's blood cannot clot in the needle (I have seen this happen) during the brief interval between the detachment of the syringe from and the attachment of funnel and tubing to the needle. Occasionally, by omitting to unclip the band round the arm, many minutes have been lost determining why, although the needle was in the vein and blood oozed briskly from it, yet the citrated blood would not run in. When connecting the needle to the tubing, take care not to jerk the needle out of the vein, and, when accomplished, secure them by a ligature, as they occasionally slip apart. A Record syringe adaptor makes this much easier.

Failure to enter the vein by needle calls for exposure by cutting. Anæsthetize and incise the skin over the median basilic vein, which is defined for $\frac{1}{2}$ in. and tied at its lower end. Place another ligature with the first knot loosely tied round the upper end of the vein (this is in readiness to retain the cannula).

Take the dissecting forceps in the left hand, pinch up about half the circumference of the vein about the middle, then with the scissors transversely snick this elevated part below the forceps, lift slightly; this further increases the opening so that the cannula (securely attached to the funnel and tubing containing saline) can be slipped well into the vein and retained by tightening the hitch of the already placed ligature. Allow the saline to flow and slowly introduce the blood, the first 2 ounces in 10 minutes, and thereafter 1 ounce every two minutes. Small soft clots sometimes form in the blood, and are separated by filtering it through a small piece of gauze over the funnel mouth. The reservoir or funnel is kept warm by hot towels; being small, the blood runs through quickly, and as the main bulk in the jar is in water at 110°F., cooling is slight.

During the injection, carefully observe the patient's pulse and appearance. Any untoward occurrence should be treated promptly. If necessary, stop; the blood can be kept warm and used later. On the other hand, a pulseless, blanched and unconscious patient may regain consciousness towards the end of it. One patient, a doctor with jaundice due to stones in the common duct, after a transfusion for secondary hæmorrhage, stated that he felt he was definitely recovering after a transfusion, whilst before it, he felt so ill he feared he was going to die. Many patients positively date their improvement from the time of a blood transfusion, whether the illness is due to hæmorrhage or severe sepsis; it certainly is a powerful aid to recovery. The apparatus is flushed immediately after use, ready for the next occasion; this avoids clotting in the tube, which might hinder or ruin the next transfusion.

Observe all the joints of the tubing and glass throughout; they sometimes slip or leak, and valuable blood has been lost in the resulting mess! Fixing the tubing and cannula (or needle) to the arm for several inches with strapping in the line of the vein will prevent the movements of a restless patient jerking the cannula from the vein. Occasionally the blood stops flowing; this may be due to an air bubble or clot in the tube or needle, or to the cannula orifice being in contact with the vein wall. The stream can be restarted by 'milking' the tube between the fingers and thumb, or by straightening the cannula in the vein; if this fails, wash the apparatus through with saline and begin again.

Transfusion, like other urgent remedies, should not be withheld too long, although it is never too late to try; a precautionary transfusion always gives beneficial results, but, if too long delayed, life-saving opportunities may be lost.

Use of Histamine in the Treatment of Pruritus

By A. CARLTON ERNSTENE, M.D.

and

BENJAMIN M. BANKS, M.D.

(Abstracted from the *Journ. Amer. Med. Assoc.*, Vol. C, 4th February, 1933, p. 325)

MILLET AND BROWN have treated patients with angioneurotic edema by repeated injections of small amounts of histamine and have obtained favourable results in a few instances. Several months ago, we administered the drug to a patient with severe generalized urticaria and constant, intense pruritus, three weeks in duration. Epinephrine, ephedrine, and calcium salts had failed to give relief. The first subcutaneous injection of 0.5 mg. of histamine resulted in complete disappearance of pruritus within twenty minutes. The wheals, however, were not appreciably affected. Eighteen hours later the pruritus returned. A second injection of the drug given at that time resulted in complete relief from itching within ten minutes and disappearance of all wheals within half an hour. Histamine was then administered twice daily for five days. Although wheals returned from time to time, their number constantly diminished, and they were not accompanied by pruritus except on two or three occasions. Each injection of histamine resulted in prompt relief from itching, when present, and gradual disappearance of the wheals. At the end of five days the patient was free of all symptoms and had only an occasional wheal. Three months later there had been no return of urticaria.

Because of this striking therapeutic result and the apparent effectiveness of histamine in relieving pruritus independently of its effect on urticarial lesions, the drug was administered not only to a small series of subjects with pruritus accompanying urticaria but also to a number of patients with itching due to other conditions. In all but one subject the customary therapeutic measures had been employed previously and without relief. The drug usually was administered in amounts of 0.5 mg. twice daily, but in one subject 1.0 mg. was given three times a day for several days and in two with bronchial asthma the first one or two injections were reduced to 0.2 or 0.3 mg. Doses of 0.5 mg. usually caused moderate to intense flushing of the face and neck with transient headache, and occasionally the subjects noticed palpitation for a few minutes. No untoward reactions were encountered, but the drug was not administered to patients with myocardial insufficiency or angina pectoris. Doses of 0.5 mg. did not precipitate asthmatic attacks in the two subjects with bronchial asthma. All patients were kept in bed for one hour after each injection of histamine.

RESULTS

Thirteen patients in all were treated, and over half of these obtained at least temporary and partial relief from itching. Five patients in addition to the case just reported had pruritus associated with urticaria. One was completely relieved for two hours after the first injection of the drug, while another reported partial relief after the second dose of histamine and was practically free of symptoms after the third injection of the drug. In both of these patients, urticaria and pruritus subsequently returned. Further treatment with histamine gave partial relief in the first but was ineffective in the second. In one other subject with urticaria, the symptoms almost completely disappeared during the period of treatment, but improvement occurred so slowly that the possibility of spontaneous convalescence must be considered.

Seven of the thirteen subjects treated with histamine had pruritus due to conditions other than urticaria, and four of these were benefited by the treatment. One patient with pruritus vulvæ, three years in duration, obtained lasting and practically complete relief from

itching. Another, who had had severe pruritus of undetermined etiology in the crural regions for one year, was almost entirely free of symptoms for three weeks after four days of treatment. Partial relief from itching was obtained in one subject with severe, generalized dermatitis of unknown cause, eighteen months in duration, and in another with pruritus due to kraurosis vulvæ, seventeen years in duration. The three patients in this group who failed to obtain relief from histamine all had pruritus ani.

Favourable results from the oral administration of ergotamine tartrate in the treatment of urticaria have been reported and the drug has been employed successfully by mouth as an anti-pruritic agent. Several of our patients were given ergotamine tartrate (Gynergen) by mouth in doses of 1 mg. three times daily for five days either before or after treatment with histamine. In none was a favourable therapeutic response observed.

With the exception of one subject with urticaria, all the patients who were benefited by treatment with histamine showed distinct improvement or were almost completely relieved of pruritus after the first one to three injections of the drug.

No explanation is available for the favourable therapeutic responses obtained nor is it known why histamine should be effective on one occasion and subsequently fail to relieve a relapse of symptoms. Millet and Brown have suggested that repeated injections of small amounts of histamine produce a state of tolerance to the drug and that this is accompanied by a diminished reactivity of the skin. This, they believe, explains the therapeutic effect of the drug in certain patients with angioneurotic edema. They, however, employed much smaller doses of histamine than were used in the present investigation. No evidence of diminished sensitivity to histamine was observed in our patients, and the prompt relief of symptoms in the favourable cases seems to indicate that the results were due to some other mechanism than a change in tolerance to the drug. The direct effect of the drug on the minute vessels of the skin may be the responsible factor.

The results obtained in the present study warrant further investigation of the value of histamine in the treatment of pruritus. This report is submitted in the hope that other investigators may have an opportunity to employ the drug, so that its therapeutic effectiveness may be evaluated by observations in a large number of patients. It would be of interest to observe the effect of the drug on the pruritus of such dermatologic conditions as lichen planus and pityriasis rosea and on itching associated with jaundice, uremia, lymphoblastoma and leukemia.

SUMMARY AND CONCLUSIONS

(1) Histamine was administered subcutaneously, usually in doses of 0.5 mg. twice daily, to six patients with pruritus associated with urticaria and to seven subjects with pruritus due to other conditions.

(2) Three of the six patients with pruritus accompanying urticaria were promptly benefited by the treatment. In one of these, lasting and complete relief from itching was obtained. In the other two, complete or practically complete relief was followed by a relapse of pruritus. Subsequent treatment with histamine failed to cause improvement in one of these and was only partially effective in the other.

(3) Four of the seven patients with pruritus due to conditions other than urticaria were improved by treatment with histamine. One patient with pruritus vulvæ, three years in duration, obtained lasting and practically complete relief from itching. One patient with pruritus of undetermined etiology in the crural regions, one year in duration, was almost completely relieved of his symptoms for more than three weeks. Partial relief of itching was obtained in one patient with generalized dermatitis of unknown cause and in another with kraurosis vulvæ. The three patients in this group who received no benefit from the treatment with histamine all had pruritus ani.

(4) Five patients were given ergotamine tartrate by mouth in doses of 1 mg., three times daily for five days, either before or after treatment with histamine. In all, ergotamine failed to relieve the itching.

(5) The results of the present study warrant further investigation of the value of histamine in the treatment of pruritus.

The Treatment of Auricular Fibrillation and Flutter

By THOMAS F. COTTON, M.D., C.M., F.R.C.P.

(From the *Practitioner*, June 1933, Vol. CXXX, No. 6, p. 698)

THE discovery of the action of digitalis in heart disease by Withering more than 150 years ago was a clinical observation which must be reckoned a landmark in the field of medical science and practice. The chance information which he had obtained from a family recipe proved a turning point in the history of the treatment of heart failure. The experience of this acute clinician established on a secure foundation a drug which is now recognized as satisfying the exacting standards required of a specific remedy. He reveals the spirit of scientific rectitude which guided him in his investigations, when he writes in a letter to a friend concerning the use of digitalis: 'It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature, and a faithful observer with an eye of tolerable judgment cannot fail to delineate a likeness. The latter will ever be subject to the whims, the inaccuracies, and blunders of mankind.' After ten years' experience he published his results in a memorable treatise which will always remain a milestone in the story of digitalis therapy. Although impressed by the effect of digitalis as a diuretic he realized that it had a definite action on the heart. His recommendation to give it in sufficiently large doses until it acts on the kidneys, the stomach, the pulse, or the bowels, is advice which could not be improved upon at the present time. For more than a century no progress was made in the treatment of heart disease with digitalis. The great advance in our knowledge of its use came when Mackenzie by clinical bedside observations discovered the specific action of the drug in what we now know to be auricular fibrillation. Clinical experience in the treatment of auricular fibrillation in its relation to heart failure has proved the value of his work.

The most critical moment in the history of a cardiac malady is the onset of congestive failure; the symptoms are characteristic, the clinical effect profound, and the causal mechanism is in the majority of cases closely related to a disorder of function produced by fibrillation of the auricles. With the onset of auricular fibrillation the auricles are virtually paralysed, rapid and irregular impulses are transmitted to the ventricles, and the contractions of these chambers are rapid and grossly irregular. This disordered action of the ventricle places a heavy burden on the heart muscle, and when there is underlying myocardial disease symptoms and signs of muscle weakness develop rapidly and cardiac failure is imminent in untreated cases. This disordered rhythm may occur in paroxysms lasting a few minutes, several hours, or occasionally days before the normal rhythm is restored. In the intervals between the attacks there may be no symptoms referable to the heart, and if the myocardial defect is slight the attacks do not lead to serious consequences. Infrequent and short paroxysms are not disabling and therefore do not require special treatment. They are sometimes related to an infective process, and when this has been controlled the attacks may not recur. Paroxysms of auricular fibrillation are a common complaint in young subjects with rheumatic heart disease, particularly in those with mitral stenosis; in older patients with degenerative changes in the myocardium and arteries; and in a well-defined group with thyrotoxicosis.

The main object of treatment in the attack is to make the patient comfortable until the normal rhythm is restored; reassurance as to the nature of the seizure is often required, and a sedative will help to remove a natural anxiety. A chloral hydrate mixture in 10 grain doses, repeated at four or six hourly intervals three or four times, is useful for this purpose. Chloralamide in cachets, gr. 10, repeated in the same way is equally effective in calming the patient. An ice-bag applied to the precordium may relieve the discomfort felt in the region of the heart. Firm pressure on the carotid sinus over the carotid artery below the angle of the jaw for ten or fifteen seconds may release a mechanism, through the vagus nerve, which can terminate the attack. If vomiting is induced the paroxysm may be shortened. Quinidine sulphate gr. 3, given every four hours, is the only drug known to have a specific effect in controlling this disturbance of rhythm. Digitalis should be withheld as it may establish a chronic state of fibrillation. A prolonged rest is not required after the normal rhythm has returned unless symptoms of heart failure have developed during the attack. Quinidine may be prescribed between the attacks for its effect in lengthening the intervals and shortening the duration; the dose is gr. 3 t.d.s.; if necessary it can be increased to gr. 15 in the twenty-four hours; a good practice is to prescribe the extra gr. 6 to be taken at bedtime; the patient need not be kept at rest on this dosage.

When auricular fibrillation has lasted for a longer period than ten days it will not revert to a normal rhythm spontaneously, and is a chronic malady. This rapid and irregular action of the heart when established is the chief cause of congestive failure and is always a serious condition in untreated cases. Symptoms of heart failure develop rapidly in those with advanced structural disease, such as mitral stenosis with much enlargement, hypertensive heart disease, and coronary atheroma. In others without chronic disease of the heart muscle symptoms of myocardial exhaustion may be delayed and the circulation well maintained for a long period.

The object of treatment is to relieve the heart of the heavy task which the rapid ventricular rate produced by the fibrillation has imposed on the ventricles. The slowing of the increased ventricular rate can be obtained by giving digitalis in doses which are large enough for the drug to accumulate in the tissues of the body. The usual practice is to give a drachm of the tincture daily for five days or a week, when the ventricular rate may be expected to fall to 70 or 80; at this level the dose should be halved, and continued so long as the rate does not fall below 60. Profound slowing, with coupling, nausea, vomiting and diarrhoea, as evidence of over-dosage, are indications for withdrawal of the drug and complete rest. When these toxic effects have disappeared, digitalis control can be resumed in the amount required, and given as a maintaining dose if the heart rate reaches 90 per minute at rest. Gastric symptoms may be avoided by prescribing the drug well diluted and after food. The patient should always be kept at rest when digitalis is given in large doses during the initial stages of the treatment. It is sometimes necessary to obtain a quick response and a rapid slowing of the heart by giving the drug in massive doses. The dosage in these circumstances for an adult with body-weight of 140 lbs. is 1½ to 2 drachms of the tincture in a single dose, and repeated twenty-four hours later if the rate remains high, followed by 20 to 30 minims daily. Massive dosing is dangerous if there is digitalis in the body at the time, and the patient cannot be kept under close observation, for the toxic effect may be rapid and produce fibrillation of the ventricles and sudden death. The daily administration of 20 minims of the tincture is a minimal maintenance dose for an adult; a smaller dose is not sufficient to control the rate, for a larger amount, averaging 20 minims, is destroyed daily by the body tissues. The white Nativelle's granule digitalin, gr. 1/240, is the equivalent of about 20 minims of the tincture, and is a convenient

and reliable preparation. The tincture of strophanthus is sometimes prescribed when digitalis is not tolerated. The initial doses are 20-30 minims daily. Compared with digitalis it is an unsatisfactory drug and is rarely required as a substitute. Strophanthin can be given in case of urgency. An intravenous injection of gr. 1/250 in 1 drachm of saline and repeated in two hours produces a rapid slowing of the ventricles; it should precede and never follow digitalis administration. The dosage of digitalis or strophanthus can be determined with a considerable degree of accuracy by giving the patient the quantity that makes him most comfortable. The ventricular rate should not be lowered below 90 when there is fever, as the cumulative effects of overdosage can occur if lower rates are maintained.

Our main objective in treating auricular fibrillation is the control of the heart rate. It is possible to obtain this object in some patients by restoring the normal rhythm with quinidine. The results are dramatic, and there is very little risk in selected cases. The most suitable for quinidine therapy are those presenting few signs of structural disease, with no enlargement of the heart and no valve disease. This drug should not be given if there is much enlargement, congestive failure, or a history of hæmoptysis. Quinidine may have to be prescribed in large doses up to 30 grains daily and continued for a week or longer before the fibrillation is replaced by a normal rhythm. Absolute rest in bed is essential, until the fibrillation is abolished or the treatment discontinued; it is desirable to keep the patient in bed for a fortnight after the normal rhythm has been restored. If the fibrillation persists after ten days of treatment the daily administration of quinine, gr. 30, may be continued for a further period of a week or ten days, but is not likely to be effective in restoring the normal rhythms. The initial dose should be small, in case there should be any idiosyncrasy for this drug; gr. 3 the first day, gr. 6 on the second day, and on the third day gr. 6 three times daily, and afterwards gr. 30 evenly spaced over the twenty-four hours. When the rhythm has returned to normal the dose should be reduced to gr. 6 two or three times daily for a week, and afterwards gr. 12 daily for a month or longer.

Auricular flutter is a disorder of the heart's rhythm caused by the rapid and regular beating of the auricles with the rate between 260 and 320 to the minute. The ventricular rate is increased and is usually half the auricular rate, i.e., 130 to 160 per minute. Conspicuous rapid and regular heart action which is persistent and is unaffected by change of posture or exercise is a characteristic feature of this condition. When the ventricles beat rapidly and irregularly, as they may do, it is difficult to distinguish auricular flutter from auricular fibrillation without the aid of an electro-cardiogram. The two conditions closely resemble one another in their causal mechanism. In both there is a disorder of rhythm caused by a circulatory wave in the auricles; in fibrillation the wave travels at a more rapid rate, and takes a more irregular course. This circus movement in the auricles is responsible for the rapid contraction of the ventricles, and the clinical effect resulting from the increased ventricular rate. In patients with auricular flutter, as in those with auricular fibrillation, a heavy load is thrown on the ventricles, and the object of treatment is to relieve the heart of this extra work by slowing the ventricular rate. This can be done by giving digitalis in sufficiently large doses to produce the required slowing of the ventricles, and by continuing the use of this drug in doses that will maintain a slow ventricular rate. This remedy has a specific action in flutter as in fibrillation, and in the general management of the cases the rules governing its administration are the same. The initial doses are heavy, a drachm a day of the tincture for a week, followed by a daily maintenance dose of 20-30 minims. When the rate of the ventricles has reached 70 or 60, the heart may become grossly irregular with the onset of auricular fibrillation, and if the drug is discontinued at this stage the fibrillation

may be of short duration and the normal rhythm permanently restored. In the majority of treated cases chronic fibrillation is established and the ventricular rate can be controlled by resuming treatment with digitalis. In some, if the patient is kept digitalized, the flutter persists, a high grade of auriculo-ventricular block is produced, and the ventricles beat at a slow rate, and heart failure can be arrested.

Quinidine can be employed with the object of restoring the normal rhythm, and is sometimes successful, but in most cases is an unsatisfactory remedy. The dosage and the management of the case is that of auricular fibrillation.

Paroxysmal flutter is rare as compared with paroxysmal fibrillation, but the treatment is the same and need not be described.

Auricular fibrillation is a disorder of rhythm frequently observed in thyrotoxic subjects. The treatment is that of toxic goitre. A normal rhythm returns after a thyroidectomy in about half of the cases so treated. If after the operation fibrillation persists a normal rhythm can be restored with quinidine. Treatment with quinidine before the operation is rarely successful. Digitalis should be given before operation if the ventricular rate is high and congestive failure imminent. It is only in exceptional circumstances and when the patient is moribund that auricular fibrillation contra-indicates thyroidectomy.

The Toxæmias of Pregnancy

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The toxæmias of pregnancy may be classified into the following groups:

- (1) Pernicious vomiting of pregnancy.
- (2) Nephritis complicating pregnancy.
- (3) Low-reserve kidney.
- (4) Pre-eclamptic toxæmia.
- (5) Eclampsia.

It is generally recognized that the toxæmias of pregnancy (apart from those of purely nephritic origin) are closely related to one another and that the underlying cause is a complicated disturbance of metabolism.

PERNICIOUS VOMITING

The simpler nausea of pregnancy without vomiting may be due to various factors—neuroses, displaced uteri, cervical erosions, adhesions, or constipation. It is frequently checked by suggestive measures, and the success of such measures would seem to prove that the condition is not essentially a pathological one.

One of the functions of the placenta is to store glycogen for the growing fetus until the foetal liver is able to store its own reserve carbohydrate, and, during this period, it is the glycogen of the maternal liver upon which it draws for its supply. At the end of the third month, the time vomiting ordinarily ceases, the foetal liver is formed and able to store its own glycogen, and then, in ordinary circumstances, the drain on the maternal liver should cease. The continued and increased demand for glycogen on the part of the rapidly growing fetus drains the glycogen content of the maternal liver. True hyperemesis is a condition of uncontrollable and pernicious vomiting sustained by a vicious circle—vomiting, starvation, acidosis. The acidosis which is so prominent a factor in the last stage of pernicious vomiting is not only a result of the intolerance of the stomach for food, but tends to increase that intolerance and so to prolong the nausea and vomiting. The gastric elimination may give rise to an alkalosis, a corollary of the cerebral oedema, the cause of headache, dullness, stupor and convulsions in fulminating cases of hyperemesis, or acute yellow atrophy, showing the ætiological relationship between the toxæmias.

In early pregnancy the carbohydrate deficiency results from a combination of a low carbohydrate-intake on the part of the mother, plus the extra burden of foetal requirements. Almost invariably, mothers report a preference for protein foods and an indifference to or even dislike for carbohydrates, especially sweets. Sometimes they diet to reduce their weight. If a diet rich in carbohydrate is supplied the foetal glycogen demand from the maternal liver, as the glycogen store-house of the body, can be met. Glucose will apparently check nearly all the toxæmias of pregnancy in their early stages and will benefit remarkably many in the later stages. Glucose infusion not only corrects the existing carbohydrate deficiency but restores and stimulates the liver cells which have been destroyed by the toxæmia.

Indifference to the vomiting of pregnancy, looking upon it as a natural physiological consequence of the pregnant state, has led to many catastrophes. Too many women are themselves prone to accept it as the inevitable consequence, and often, before it is realized, a grave pathological state has developed from what was originally considered only a minor discomfort. Preventing the simple from becoming the complex by careful antenatal watching, and treating the condition in its incipency, should therefore be the criterion of any system of treatment which is advocated. It is possible, in all circumstances, at least to make the patient more comfortable.

Treatment.—Isolation, early, in a hospital is, of course, most desirable, but if kept at home the patient should be in the brightest and sunniest room, as far away from the kitchen as possible. She should be relieved of cooking and should rest in bed in the morning. She should sleep alone. The anxious husband, family, and visitors must be excluded. Complete confidence in the doctor and nurses must be obtained, and co-operation and the exercise of the patient's will-power assured by the strongest encouragement. A complete physical examination is made and appropriate treatment instituted for any abnormal pelvic condition. The CO₂ (which is generally low, and the blood predominate) are estimated.

No food should be administered by mouth for forty-eight hours, so as to rest the stomach. Glucose, preferably 250 c.c. of a 25 per cent glucose-saline solution per hour, should be given intravenously at body temperature, morning and night, beginning immediately on admission. The stronger the solution of glucose, the more rapid and lasting are the effects; the more strongly hypertonic favours a more rapid interchange between the tissues and the blood. Normal saline, 500 c.c., may be given daily by hypodermoclysis, or intravenously if marked dehydration is present. A cleansing enema is given every morning. Rectal instillations of glucose (drams 4), sodium bromide (grs. 60), and saline to make 6 ounces, are given slowly every four hours. Small blood transfusions of 300 c.c. of human blood by the direct method, to which may be added 500 c.c. of normal saline, have given satisfactory results, when glucose fails to produce improvement. Luminal, grs. 1½, is given by mouth or hypodermically, to assure sleep at night, or to allay nervousness during the day. The fluid intake and output are measured daily. A duodenal nasal tube (which may be kept in place for days), with the injection of 10 per cent Karo syrup and skimmed lactic acid milk or butter-milk; or 5 per cent Dryco, with or without luminal, can be used, beginning with 50 c.c. per hour up to 300 c.c. per hour, according to the patient's tolerance (glycosuria or diarrhoea).

With the patient's assurance of retaining certain articles of diet after a usual favourable response within two or three days, when the vomiting lessens and the patient begins to feel hungry, a dry diet is gradually begun, consisting of buttered toast, rice, potato, jam, marmalade, baked apple, fruit juices, advancing to chicken or fish and some vegetables or broth. Ginger ale or butter-milk is sometimes retained. At this stage,

glucose may be discontinued intravenously and continued by mouth and rectum. A laxative may supplant the enema. The patient is advised to refrain from fatty foods (which are incompletely oxidized) and is encouraged to drink at least 1½ quarts of fluid daily. Milder cases are treated with a high carbohydrate diet of solid food, in small meals at frequent intervals, with resting between feedings. A glucose mixture consisting of 1 lb. of glucose plus 1 quart of water, with the juice and chopped-up skins of two lemons added, boiled 5 minutes, strained, and taken during the twenty-four hours, contains 1,000 calories and is beneficial.

The injection of 10 c.c. or more of the husband's blood intramuscularly into the patient's buttocks, twice weekly or oftener, sometimes helps to alleviate the vomiting. The theory is that the blood of the foetus may be of different type from that of the mother but the same as the father, so that the husband's blood renders the mother, by desensitization, immune to the foreign protein. Gastric lavage may be resorted to after each vomiting, if the patient vomits persistently. A good response is often found. Removal of the vomiting pain sometimes aids, so that if the patient vomits she must do so on the floor or on the edge of the bed.

Ovarian extract (whole ovary), or corpus luteum, in conjunction with the other routine, is used, in doses varying from a gr. 5 tablet every three hours to an intravenous injection of 1 c.c. or more every two hours, on the assumption that the ovary sometimes fails to produce a hormone stimulating the excretion of pituitrin into the cerebrospinal fluid, which, entering the circulation, helps to empty the uterus and to start the flow of milk; as a result of this hormonal deficiency, toxæmia follows, which may be neutralized by saturation of the patient with ovarian extract.

However, all cases of pernicious vomiting cannot be relieved by injections of glucose; sometimes all measures fail. In such cases prompt evacuation of the uterus must be resorted to. It may be suggested that if after four days' intensive glucose therapy, followed by four days of duodenal treatment, a decided improvement is not evident, then interruption of the pregnancy should be justifiable. The danger signs are a rising pulse rate, a falling blood pressure, a dry tongue and blurred vision. The daily urine output should be about 40 oz., of 1010 specific gravity.

Success depends upon instituting intensive treatment early, before dehydration has advanced too far. Laboratory investigation of the last few years, plus the brilliant results obtained through the administration of glucose in the various toxæmias, suggests more strongly than ever that some carbohydrate metabolic disturbance is at the root of the trouble.

NEPHRITIS IN PREGNANCY

Nephritis in pregnancy, which usually manifests itself during the later years of the child-bearing period, may be a very serious complication, resulting from a persistent renal or vascular disease which has reduced the renal reserve, and it may be complicated by cardiac disease, pyelitis, anaemia, thyrotoxicosis, acute infections or obstetric difficulties. The onset is insidious, often at about 5 months, and may begin with a pronounced rise in arterial tension preceding the albuminuria, and diminished output, with headache, nausea and vomiting, a sharp gain in weight, blurred vision, indigestion, epigastric pain and oedema. The essential characteristic of a true nephritic toxæmia is the frequency with which the renal function is permanently impaired (80 per cent after 3 years), each succeeding pregnancy leading to further renal degeneration and arteriosclerosis. The prognosis is grave.

Treatment.—The total urine output for twenty-four hours is measured and charted. An Esbach estimation is set up daily and the blood pressure taken morning and evening. The fluid balance is regulated. The amount of fluid by mouth is placed on a minimum or withheld entirely for the first twenty-four hours accordingly, and then given in quantity not exceeding

the total urinary output for the previous twenty-four hours. Thus the water balance is maintained by placing the level of the fluid intake at the point of maximum renal efficiency, so lessening the quantity available for oedema. The fluid balance may be maintained at the twenty ounces level and gradually increased as the output rises, forty ounces being the maximum required to meet all bodily needs. The giving of large quantities of fluids to lessen the toxæmia has been abandoned in favour of dehydrating measures, in conjunction with small fluid intake in an already water-soaked body, resulting in renal improvement and early mental restoration.

Dehydration is promoted by the giving of 50 c.c. of a 50 per cent glucose solution intravenously, repeated in 6 hours if necessary, and by purgation with $MgSO_4$, 1 or 2 ozs. daily, by the mouth, to remove the excess tissue fluids. The patient is weighed daily, and her weight checked up with the urinary output, giving the gain or loss thereby in terms of fluid. Later a salt-low diet is maintained by curtailing the use of salt at the table and avoiding salty foods. Carbohydrate metabolism requires two-thirds more water than that of protein, so that excessive carbohydrate should be eliminated, such as sugar, candy, ice-cream, honey, syrup, jelly and preserved fruits, leaving safely vegetables and starches obtainable in an ordinary diet. Strict fluid-balance treatment should be maintained throughout. Venesection may be done.

Failing reasonably rapid improvement, induction of labour by the gentlest method should be done. In the presence of a definite chronic nephritis, radical treatment is often required. It may be advisable to terminate pregnancy and prevent if possible further pregnancies, by Cæsarean section and tube resection.

LOW RESERVE KIDNEY

The low reserve kidney is a mild intoxication late in pregnancy with only slight arterial hypertension, moderate albuminuria, moderate oedema and urine of low specific gravity—a renal fatigue—in a healthy organ, temporarily insufficient functionally.

Treatment.—Dietary, with $MgSO_4$, sees the early return to full normal health. However, the time to prevent kidney strain from pregnancy is not after a chronic nephritis has become severe but while it is still mild in character or in its incipency, for then only can we hope to be of much assistance to our nephritic patients.

PRE-ECLAMPTIC TOXÆMIA

Patients with definite signs of hypertension, oedema of the extremities, headache, dizziness, blurred vision, nausea and vomiting, epigastric pain, restlessness, mental disturbances or anguish, jaundice or hæmorrhagic tendencies, together with diminished highly albuminous urine, are in this apprehensive group.

Treatment.—(See treatment for nephritis above). The total urinary output for the 24 hours is measured and charted. Daily Esbach and blood pressure estimations are made. The water balance is maintained. Dehydration is carried out with glucose and magnesium sulphate. The weight is checked daily. A spinal puncture is done, 45 to 100 c.c. are drawn off at intervals of 4 to 6 hours if no improvement occurs in 24 hours, with headaches and cerebral symptoms persisting. Venesection may be done. A salt-low diet is instituted later if the progress is favourable, if not induction or Cæsarean.

ECLAMPSIA

It has been shown that eclampsia, which is a syndrome rather than a disease, is primarily related to carbohydrate deficiency and glycogen depletion of the liver, due to foetal demands. The convulsive seizures occur at levels designated as relative hypoglycæmia, caused by the sudden rapid drop in blood sugar, it may be a few minutes' time, followed by a temporary rise, the usual physiological response of the liver to muscular convulsive activity. (Normal blood sugar is 90-120 mg.

per 100 c.c.; sometimes it drops 50 to 80 mg. suddenly). A tendency exists towards remissions to lower levels, so that the general trend of the sugar content of the blood is downward, obviously the effect of exhaustion of reserve glycogen stores in the liver.

The search for a common factor responsible for the physiological changes in the brain which may tend to precipitate convulsive seizures finds a fundamental relationship between fluid (oedema), poor oxygen supply, and the acid-base variations with their local effect on capillary circulation and permeability, and increased intracranial pressure, the control of which may be assisted by the establishment of a proper 'water metabolism'.

Treatment. Prophylactic.—Prenatal care stands out as one of the greatest contributions in the advancement of the therapy of the toxæmias. Improvement in results will come from active interference before the convulsive stage in the toxæmic patients. It is well to assume that every albuminuric or hypertension patient is a potential eclamptic who should have ceaseless watching in her prenatal period and pre-conclusive interference to prevent the convulsive phase.

Having decided by complete examination that the patient is in good health and a fit future mother, she is watched carefully for any signs or symptoms of toxæmia. Should she develop a moderate hypertension, a trace of albumin or a slight oedema, she is placed on a moderate low-meat modified carbohydrate and salt-poor diet, is given magnesium sulphate; her weight is watched; she is advised to rest several hours daily and to return at weekly intervals. If improvement is not shown (if blood pressure is 140 or over with albuminuria), she should be put to bed or hospitalized.

Nursing care.—The eclamptic patient must be treated very gently, scarcely touched at all, and the tongue protected. The utmost quiet must be observed by the nurse, who should be constantly with the patient. The patient may be blindfolded and have her ears plugged with cotton-wool, to lower her response to external stimuli and thus diminish the likelihood of further convulsions. The room should be kept dark and warm, the patient must be kept warm, even perspiring. Her position should be changed four to six times or more daily, to avoid hypostatic pneumonia, with the nose and mouth lower than the bottom of the chest. Sometimes suction or an inserted tracheal tube is used to relieve pulmonary oedema (which is often a cause of death).

Medical treatment has for its object the control of convulsions until a spontaneous delivery takes place. Better results are obtained by conservative than by more radical active interference and immediate operative delivery. A hypodermic injection of sodium-luminal, 2 or 3 grains, is given immediately, and repeated in two hours if necessary, or morphia, gr. $\frac{1}{4}$ or $\frac{1}{2}$ hypodermically, which is well tolerated, may be given, and gr. $\frac{1}{4}$ may be repeated with each succeeding convulsion until the respirations are 10 to the minute. Magnesium sulphate, 20 c.c. of a 10 per cent solution, may be given intravenously immediately after the first convulsion, and may be repeated every two hours or more until the convulsions are controlled or the blood pressure lowered. It acts as a sedative, a diuretic and detoxicant, and decreases the intracranial pressure and oedema. The magnesium sulphate may be continued after delivery, if necessary.

The symptomatic treatment of the convulsions having been accomplished by sedatives, the use of glucose is directed towards the underlying cause of the disease. At the earliest opportunity a glucose intravenous injection of 50 c.c. of a 50 per cent solution is given and repeated every 3 to 4 hours if indicated. The enormous consumption of energy incidental to the convulsions requires fuel to replace the depleted stores. The hypertonic glucose solution has a liver-sparing effect, combats the glycogen depletion of the liver, draws the fluid out of the tissues, stimulates diuresis, lessens the cerebral oedema, reduces the intracranial pressure and

thereby helps to control the severity and the number of the convulsions. It is supportive and detoxicant. Insulin may be indicated in coma or semi-consciousness or diabetics following a convulsion with low carbon-dioxide (of 30 or below), and an elevated blood sugar.

Spinal puncture is done as early as possible—complete drainage (45–100 c.c.), with the head raised at an angle of 30 degrees—and is repeated in 4 to 6 hours, failing marked improvement. Venesection of 700 c.c. or, in proportion, if the blood pressure is over 170, may be done until the pressure falls to 150. It lowers the blood pressure and assists the heart and lungs. Magnesium sulphate, oz. 2, by mouth, if practicable, is also given, to withdraw fluid from the blood reclaimed by the intravenous glucose, and thus hasten the re-establishment of body water balance. Colonic irrigations, hot packs and gastric lavage are considered.

Fluid balance.—All foods and fluids are withheld for 24 hours; then the fluid intake is given, some ounces less than the previous day's urinary output. Gradually a fluid balance is thus established and maintained on a greatly restricted fluid intake. The principles involved in the water balance of the body should receive most careful attention, as the results attendant upon it are striking.

Oxygen is given liberally, early, as a routine, by inhalation after each convulsion until breathing is normal, and continued until cyanosis disappears. It retards autolysis of the liver and aids recovery, besides acting as a cardiac nervous stimulant. Blood transfusion is given for hæmorrhage.

The temperature, pulse, respiration and blood pressure are recorded hourly. The total daily urinary output and the intake of fluids are measured, and the weight is recorded daily. An Esbach estimation is set up daily.

Diet—later, fluids, fruit juices, fruit, glucose mixture, milk, water liberally.

Rest in bed.

Sometimes small blood transfusions help or blood transfusion or serum from a recovered eclamptic. The reinfusion of autogenous washed corpuscles, with removal of the supposedly toxic plasma is reported to help. Liver extract may be given.

Interference with pregnancy may be instituted if labour supervenes; delivery should be preferably by forceps, with nitrous oxide and oxygen used sparingly, or, best, with local and spinal anaesthesia, with narcotics or ether, with as little disturbance as possible. Otherwise, labour should be hastened, and induced in the most conservative manner in all cases, just as soon as the convulsions have been controlled as otherwise, damage to the organs endangers the patient's life. Induction of labour may be accomplished by medical means, rupture of membranes, bougie, bag, version, or forceps, if no response to treatment is made. Otherwise, a Caesarean section is performed in selected cases only where urgently demanded as in the rapidly advancing case and especially in a severely ill rigid primipara with no cervical effacement where there is no response to medical treatment.

Post-partum treatment is of vital importance for the patient, who requires constant care and close observation. The diet is restricted to a proper fluid balance—dehydration by forced saline purgatives and enemas are important, with a daily check-up of the blood pressure and urinalysis.

Prognosis.—The outlook for a successful normal pregnancy in eclampsia may be less favourable than is generally supposed, but with strict antenatal care, future attempts at child-bearing need not be discouraged. The patient, however, should be carefully observed in the interval. Women with a persistent systolic pressure of 150 and diastolic above 100 at the beginning of pregnancy are not likely to go through successfully; in such, abortion must be considered. Otherwise, if a woman wishes to run the risk, rest in bed for weeks or months may be required. The behaviour of a woman's cardiovascular-renal system in pregnancy, together with

the promptness with which improvement occurs following delivery, gives to the physician a valuable hint as to what might be expected of it under subsequent strain.

Some Recent Developments in Anaesthesia

By F. B. PARSONS, M.A., M.D., M.R.C.P.

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THE BARBITURATES

THREE derivatives of barbituric acid have been used extensively as basal narcotics. These are sodium amytal, nembutal and pernocton and it is stated that they have the following points in common: (1) There may be very considerable variation in the observed effects when given in the same dose to the same species; in other words, the variability of action has made it difficult to secure an accurate scale of dosage. (2) In hypnotic doses they may produce respiratory and circulatory depression. (3) During the processes of destruction and excretion, certain products are formed which may produce mental disturbances and restlessness. These may persist during the period of excretion which may occupy several days.

Sodium amytal.—This is a white crystalline powder which is given intravenously in aqueous solution. The method of administration is peculiar; the solution is freshly prepared and is then injected at the rate of 0.1 gram per minute until the patient fails to answer to the spoken word. When the injection is completed, inhalation anaesthesia is superimposed as with avertin and both gas and oxygen or ether may be used for this purpose. Sodium amytal depresses the cardiovascular system more than avertin does; the systolic blood pressure falls to 30 mm. Hg. or more; the diastolic 15 mm. mercury or more and the pulse rate always rises considerably. Respiration is depressed to a less extent than is seen with avertin but, on the other hand, reflex excitability is at a much lower level.

Nembutal.—Nembutal (sodium-ethyl-methyl-butyl barbiturate) is more toxic than sodium amytal and therefore can be given in smaller doses to produce a similar degree of narcosis. As the dose is smaller, detoxication is accomplished in a shorter time and therefore the recovery period is not nearly so long as with sodium amytal, the recovery period of which may extend to 24 hours. This drug can be given either intravenously or by the mouth; the former method is identical with that employed for sodium amytal, but as the dose is only half as large, administration occupies only 7 or 8 minutes. When nembutal is given by the mouth an attempt is made to correlate the dose with the body weight but this does not lend itself to the accurate results which can be obtained by the former method. When given by the mouth, the patient falls asleep in about 20 minutes and there may be narcosis in a further 10 to 20 minutes. There is usually nystagmus and very frequently strabismus at this stage; an effect which is common to all derivatives of veronal in heavy dosage. There is usually some twitching of the limbs also a peculiar flickering of the eyelids. Muscular relaxation is not nearly so marked as with avertin, but there is a greater degree of insensibility. For example, when a patient has been given the appropriate dose of nembutal by the mouth, induction can be completed and anaesthesia maintained with open ether with very little change in the rate or amplitude of respiration. This function is not greatly depressed by nembutal, the only apparent difference being the decrease in the depth of respiration. The fall in blood pressure ranges from 20 to 30 mm. Hg, but this tends to rise again in a short time.

Regarding after-effects, the recovery period after oral administration is comparatively short and seldom extends beyond three hours. Not infrequently excitement occurs during this time and involuntary movements of the limbs, together with shouting may be observed.

The incidence of post-operative vomiting is no greater than with avertin. With intravenous injection Boyd states that the full hypnotic effect, when produced, lasts 4 to 5 hours and for a further 12 or more hours the patient is peacefully asleep.

O'Sullivan and Craner advise the use of nembutal and chloral hydrate as an analgesic in childbirth. Three grains of nembutal are given by the mouth followed by 30 grains of chloral hydrate. Either or both of these can be repeated in modified doses after 2 hours and additional doses may also be given. Usually a painless labour results, but this process may be prolonged and may be succeeded by restlessness.

Pernocton.—Pernocton, the last member of this series, is the sodium salt of secondary beta-bromallyl barbituric acid, and it is issued in ampoules already dissolved in water. Its hypnotic effect is comparable with that of nembutal but it is effective in smaller dosage. The average quantity of pernocton necessary to produce narcosis is 4½ grains; this amount is contained in 3 c.cm. of solution, which, when administered intravenously, at the rate of 1 c.cm. per minute, can be injected in

3 minutes and still further shortens the induction period when compared with nembutal. Administration of pernocton is conducted in precisely the same manner as with the two previous drugs and unconsciousness supervenes before the needle is withdrawn. Pernocton anaesthesia resembles that produced by nembutal, but it is stated that vomiting and excitement are prone to occur. The recovery period is said to be from two to six hours.

It is probable that nembutal is the most commonly employed barbiturate at the present time. The oral method of administration is most convenient, but it is difficult to form an accurate estimation of the necessary dose. The intravenous route gives excellent results and is preferred by many administrators, but according to the Council of Pharmacy and Chemistry of the American Medical Association it is subject to the objection that all barbiturates require large quantities of alkali for solution and, therefore, they will not remain in solution in the blood stream. They are believed to be precipitated and to circulate as foreign bodies in the colloidal state.

Reviews

ENDOCRINE MEDICINE.—By W. Engelbach, M.D., F.A.C.P., B.S., M.S., D.Sc. Volumes I, II and III with an Index Volume. Baltimore: Charles C. Thomas, 1932. Vol. I:—Pp. xxviii plus 460, with 139 figures. Vol. II:—Pp. xviii plus 473, with 109 figures. Vol. III:—Pp. xxiv plus 862, with 255 figures. Index:—Pp. vi plus 117. Price.—the whole, £10-0-0. (Obtainable from Messrs. Baillière, Tindall and Cox, London.)

THE history of medicine of the last century closed on the bacteriological note, the first quarter of the present one on the endocrine. The endocrine fashion reached its height about seven or eight years ago, and at that time there was a tidal wave of books on the subject; many of these were valuable contributions to medical literature but the great majority consisted of an agglomeration of ill-digested facts regarding the functions of the various ductless glands and of the activities of their extracts. At that time the subject was running a risk of being choked by the weeds of poly-glandular therapy, but the last few years have seen a great advance in the subject and, what is more important, they have been a period of discovery of connecting links, and of arrangement and classification.

It is therefore a good time for a book of the nature of the one under review to appear. The author is a physician and it is from the point of view of the clinician that the book is written. By this we do not mean to suggest that it is a mere record of clinical experience; far from it, the subject is treated from the beginning. After a very short but effective history of the subject there are chapters dealing with the anatomy, histopathology and physiology of the endocrine glands. There are two important chapters on endogenous and exogenous aetiology, respectively. The next section is headed 'diagnostic procedure'; it commences with a chapter of about 50 pages on anthropometry, in which the author gives a complete account of 'normal' measurements, collected from authorities in many countries. One realizes the importance of these measurements—to which he subjects all the patients in his clinic—but one also realizes that before any conclusions can be based on them it is essential to have the normals of the race with which one is dealing. The figures he quotes are mainly collected in America and under 'nationality' the commonest entry is 'native' which one concludes means the local white race stock. The next chapter heading—*anamnesis*—drove the reviewer to the dictionary where he got little help; he

soon found however that 'past history' was what he himself would have used. This section contains further chapters on case taking. The next section deals with endocrine reactions. The chapter on hormone and specific reaction is particularly useful for reference, as it contains very concise descriptions of the functions of different hormones. The first volume closes with a chapter on the relationship of endocrine disorder and public health. The author's object is to stress the dire effect of the endocrinopathies upon the health of the public and to point out that defects in the endocrine system are amongst the most important causes of human incompetency and delinquency. There are in the next two volumes four similar chapters dealing with this same subject in specific relationship to these disorders at the four different age periods.

Space will not permit of any detailed discussion on the next two volumes. They contain four sections, respectively, on infantile, juvenile, adolescent and adult 'endocrinopathies'. There are in all four volumes—the fourth being devoted to a bibliography and indexes of names and subjects. The whole provides as complete a treatise on the subject of the endocrine glands and their disordered functions as one could want. It is encyclopedic as regards the volume of the information it contains, but it does not suffer the disadvantage of having been written by a number of authors whose ideas are not in tune.

The book is singularly free from what the English reader calls 'Americanisms'. 'Incretion' and 'incretory' are no longer new and are justifiable shortening of 'internal secretion' and its adjectival form. The reviewer was inclined to protest against 'hyposectomized', until he decided that it was a misprint (the only one he saw) for 'hypophysectomized'. The illustrations and diagrams are abundant and always useful. The reproduction of the skiagrams and histological sections are particularly good. We have two small criticisms here; the author has written the indicating letters (*e.g.*, C, cortex; M, medulla) on the photographs and in some instances it is more difficult to find the letter than it was to 'find the girl's father' in the old Christmas cracker puzzle. Also the diagram on page 144 is a little too 'kindergarten' for a book of this kind.

We cannot conclude without congratulating the publishers on their share in the production of a work that is of the highest order from a scientific, from a practical, and from an artistic point of view.

L. E. N.

SEX AND INTERNAL SECRETIONS. A SURVEY OF RECENT RESEARCH.—Edited by E. Allen. London: Baillière, Tindall and Cox, 1932. Pp. xxii plus 952, with 318 figures. Price, 57s. 6d.

The publication of this volume celebrates the tenth anniversary of the beginning of an inquiry into the problems of sex initiated by the Bureau of Social Hygiene and carried out under the control of the Division of Medical Sciences, National Research Council of America. As these researches are still being conducted the book under review is in the nature of an interim report and general summing up of the state of our knowledge on sex up to the present day.

There are nineteen chapters to which twenty-two authors have contributed, most of these hold important university appointments in the United States, and are actively engaged in research along one or more of the lines touched on in the book.

In a book compiled in this manner there is a good deal of overlapping and repetition in certain of the chapters. To some extent this is unavoidable, but it is felt that if the editor had exercised his authority a little more, and cut out some of these repetitions, it would have been an advantage.

The title of the book is somewhat misleading for it is much wider in its scope than this indicates, and several of the chapters make no reference to internal secretions at all. It appeals to the reviewer much more as a general summary of the whole subject of genetics than one limited to the influence of internal secretions on sex, and as such it will be of great value to all biologists. The mass of papers that have been consulted is enormous and the extent of the search through the literature is shown by the long bibliography after every chapter.

This publication cannot fail to be of great assistance to any one engaged on problems relating to breeding of animals, because references to all the recent work on the subject are to be found somewhere in the book, and this subject has now become so many-sided and so complicated that without a book of reference of this type it would be difficult to progress, because it would be far beyond the powers of one man to keep abreast of the literature.

Although it may be read with profit by those with only a general interest in biology, it is much more to be recommended as a book of reference to the specialist, for he will find discussed within its pages whatever problem in genetics he may be working upon, or if it is not fully discussed he will be given all the references he will require whereby to follow up his special inquiry.

P. A. M.

RECENT ADVANCES IN RADIUM.—By W. Roy Ward, M.B., B.S., M.R.C.S., and A. J. Durden Smith, M.B., B.S., M.R.C.S. London: J. & A. Churchill, 1933. Pp. viii plus 324, with 4 coloured plates and 140 black and white illustrations. Price, 21s.

THE Recent Advances series has acquired a very high reputation and this latest addition will most certainly help to maintain it. However, except in the matter of quality, this book differs from the others of the series very markedly; the excuse for the title and the justification for the procedure the authors have adopted are the same, namely, that the whole subject of radium therapy is so new that everything worth knowing on the subject is necessarily a recent advance. Consequently, the book is nothing less than a textbook on radium therapy, and a reader who has hitherto enjoyed complete ignorance in this matter need not fear being landed in the middle of a subject where he will be completely lost; on the contrary, if he opens the book at the beginning he will find the mystery of radium and its therapeutic properties slowly unravelled in a manner that would throw no burden on even a very mediocre intelligence.

The book is divided into three parts; the first part deals with the fundamentals of radium, its physics, its

selective action, the radio-sensitivity of different tissues and cells, the measurement of dosage, radium apparatus, protective measures and so forth; the second part deals with the treatment of malignant tumours in different parts of the body, region by region; and part three deals with the treatment of non-malignant tumours, and other conditions, such as uterine hæmorrhage.

The most important lesson the book conveys is that there are very great potentialities in this form of therapy, but that it will take many generations of essentially experimental clinical trials and most laborious appraisement of the results before we can hope to gauge the extent of its possibilities or to give any accurate prognoses in individual cases, but that even at the present day we have reached a stage where radium therapy should always be considered when the treatment of any operable or inoperable new growth is under consideration, and that there are certain other conditions in which it is the best form of treatment at present known to science.

There are numerous very useful illustrations distributed throughout the book; the microscopic sections are particularly well reproduced; and there are many coloured plates. A number of before-and-after photographs are included, but these provide their own justification and, though mostly, if not all, taken from the authors' personal experience, the claims they make for good results are so entirely impersonal that one's natural prejudice against this form of illustration is entirely overcome.

We can strongly recommend the book to all medical men; if they are not particularly interested in the subject now, they probably will be when they have read this book.

GENERAL HÆMATOLOGY WITH SPECIAL REFERENCE TO THE CHILD IN HEALTH AND DISEASE.

—By W. M. Feldman, M.D., B.S., M.R.C.P. (Lond.), F.R.S. (Ed.). London: John Bale, Sons and Danielsson, Ltd., 1933. Pp. 96. Illustrated. Price, 2s. 6d.

THIS series might well be called the vest-pocket monograph series, as compared with other 'pocket' series it really is very small. However the print will not be found at all trying to most readers, and in these days of large volumes it is very pleasant to have a light book in one's hand.

It was of course impossible to write a treatise on such a large subject in the small space available, and it is rather difficult to say what the author has exactly achieved. It is not a book on technique, as this is given no place, and it is not a book on blood diseases; it might be described as a student's primer on the applied physiology of the blood. There is in it much useful information very clearly expressed.

The author does not appear to have accepted the recent work on pernicious anæmia as he makes frequent reference to the excessive hæmolysis in this condition and, at least on one occasion, to toxins as the cause of this.

The book should be valuable to the student, or even the nurse, reading for an examination.

L. E. N.

BLOOD PICTURES: AN INTRODUCTION TO CLINICAL HÆMATOLOGY.—By C. Price-Jones, M.B. (Lond.). Third Edition. Bristol: John Wright and Sons, Ltd., 1933. Pp. 72, with 5 coloured plates and 7 illustrations in the text. Price, 6s. 6d.

THE name 'Price-Jones' has acquired a very firmly-established place in hæmatology. This little book of his is perhaps not so well known as the author.

It is a book for the student and general practitioner and the intending reader need not be frightened by the prospect of a volume full of curves and mathematical calculations; the book contains nothing of the kind. Price-Jones curves are given, but the whole subject of cell measurement occupies only four pages. The book is what its name suggests. Simple technique is

described and there are some very useful plates. As a small point of criticism, in the reviewer's opinion all coloured plates of blood pictures should have on the plate itself some indication of the staining method used; that this is clearly stated in the text is no answer to this criticism.

The plates are well reproduced and the general format of the book is good. It should be useful to students and general practitioners.

L. E. N.

CLINICAL OPHTHALMOLOGY FOR HOUSE SURGEONS AND STUDENTS.—By J. M. Bickerton, M.A., B.Ch., F.R.C.S., and L. H. Savin, M.D., M.R.C.P., F.R.C.S. London: H. K. Lewis and Co., Ltd., 1933. Pp. 158, with 92 illustrations including 6 plates. Price, 7s. 6d.

THIS small book has been produced with the object of providing a short course of instruction for students, because the standard textbooks are all so large.

The authors have admirably succeeded in the task they have set themselves for they have presented the subject in an eminently practical manner only giving the essentials. The book might well be used to replace the notes the student usually tries to take while attending his practical ophthalmology classes, and, being properly arranged and carefully edited, it is much more useful than the most carefully taken notes can ever be. The low price also brings it within reach of all. The penultimate chapter is devoted to formulæ which will cover the whole field of eye therapeutics in any average practice, and the last chapter is devoted to drawings of all the common eye instruments. Provided it is not looked upon as a textbook but simply as an introduction to the study of ophthalmology, it can be confidently recommended to all beginners.

MEDICINE FOR DENTAL STUDENTS.—Edited by H. A. Lucas, Edinburgh: E. & S. Livingstone, 1933. Pp. 208. Publishers:—Messrs. Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 5-10.

THE recent inclusion of an examination in medicine for the L.D.S. Eng. has made the subject of medicine of more than academic interest to the dental student. This book is a laudable attempt to provide him with the essentials of the subject.

In the preface the editor wisely remarks that ordinary textbooks of medicine fail from the point of view of dental students in being too long, while they contain too little pertaining to those special aspects of medicine which are of importance to the dental student. It is in this latter respect that this book must be tested. Twenty years ago dentistry was mainly affiliated to surgery, partly because of the part which the College of Surgeons played in sponsoring the L.D.S. and partly because the obvious extensions of dental conditions were into the domain of surgery rather than medicine. But at the present time some knowledge of medicine is almost of equal importance. The whole problem of focal infection in relation to many conditions, medical rather than surgical, make it necessary for the dentist to know something of the conditions which may be caused by dental infection. Again, such diseases as purpura, jaundice, leukaemia or agranulocytosis, which may give rise to oral infection and thus come under the notice of the dentist, have assumed a practical importance in dental surgery. The increasing use of local anaesthesia has made a knowledge of cardiac and respiratory conditions essential.

The book opens well with two chapters on infection and immunity. Then follow chapters dealing with the different systems of the body. These are of necessity brief and in some cases too brief. Thus the chapter on diseases of the blood only extends to ten pages. Yet in this section are included conditions of such practical importance as leukaemia, purpura hæmorrhagica and hæmophilia. In leukaemia, for instance, a stomatitis is of frequent occurrence. In the past it has happened that patients have been seen by the dentist with what

appears to be an ordinary type of stomatitis. The extraction of teeth has been followed by an intractable hæmorrhage resulting in death. This is a section which should be amplified considerably, and we hope that in future editions the opportunity will be taken to emphasize even more than has been done, those particular aspects of medicine which are of practical importance in dental surgery. Though brief, this book should fill a useful place and prove of much assistance to the student in preparing for his examinations.

E. H. B.

THE HISTORY OF DERMATOLOGY.—By Wm. A. Pusey, A.M., M.D., LL.D. London: Baillière, Tindall and Cox, 1933. Pp. xviii plus 224, with 32 illustrations. Price, 17s. 6d.

THIS is the first history of dermatology to appear in the English language, and as such it cannot fail to be of interest to all English-speaking medical men.

Like most histories on medical subjects it begins with the Edwin Smith papyrus, as this is the earliest written record extant dealing with medical science, and it is surprising to learn that both in this and in the famous Ebers papyrus considerable space is devoted to dermatology. It seems that the cosmetic side of the subject received more attention in those ancient days than the actual treatment of diseases though these also received attention. We also learn that among the remedies used for treatment of skin diseases 1,500 years B.C. calamine and sulphur occupied an important place.

The book is divided into chapters each of which covers a definite period of history, and, written as it is by a man who has devoted his life to the study of skin diseases and has contributed a great deal to the literature, the value of each advance is accurately gauged with the result that the complete record gives an impression of careful balance, as every noted dermatologist from Galen to Hebra receives the proportionate amount of attention to which his work entitles him.

The early chapters in which the work of the great dermatologists of the past is described are more interesting to read than are the chapters devoted to our contemporaries, but this is probably unavoidable because it is notoriously difficult to write current history on any subject. The book is, however, a valuable contribution to the history of medicine and the author is to be congratulated on the admirable performance of a difficult task. The paper, printing, binding, and the manner in which the well-selected illustrations have been reproduced, combine in the production of an artistic volume, which quite apart from the interest of its contents will be an ornament on the shelves of any library.

P. A. M.

MEDICAL ENTOMOLOGY.—By R. Matheson, Ph.D. London: Baillière, Tindall and Cox, 1933. Pp. xiv plus 489; 211 figures. Price, 29s.

THIS general textbook on medical entomology deals mainly with American insects and has therefore definite limitations as a universal textbook. The structure and natural history of the insects described is clearly and concisely recorded, but the epidemiology and the practical measures for control of some of the diseases transmitted by insects are very incomplete, especially the chapter on malaria control. The importance of dense shade as an anti-malarial measure, and the dangers attending drainage in certain parts of India appear to be unknown to the author; likewise the exact method by which petroleum oils destroy mosquito larvae.

On page 22 the lung fluke, *Paragonimus westermani*, is stated to occur in Assam and Bengal. The reviewer is unaware of any cases ever having been recorded in either of these two provinces of India.

Reference is made to the pioneer work of Knowles, Napier and Smith on the problem of kala-azar transmission with *Phlebotomus argentipes*, but the actual reference is not given although the book has otherwise

a very excellent index to authors and a well compiled subject index.

The anatomical sections are well illustrated, most of the illustrations being original.

The book is well printed and an introductory chapter gives an excellent brief account of the history of medical entomology during the past fifty years.

G. C. R.

HYGIENE FOR NURSES.—By John Guy, M.D., D.P.H. (Camb.), F.R.F.P. & S. (Glas.), F.R.C.P. (Edin.), and G. J. I. Linklater, O.B.E., M.D., D.P.H., D.T.M. & H., M.R.C.P. (Edin.). Second Edition. Published by Messrs. Butterworth and Co. (India), Ltd., Calcutta, 1933. Pp. xi plus 211. Illustrated. Price, Rs. 3-12.

DRS. GUY AND LINKLATER bring to the task of writing a book on hygiene for nurses not only a wide practical knowledge of public health but also invaluable experience gained as examiners in hygiene to the General Nursing Council.

In accordance with the modern tendency to lay emphasis on the importance of individual hygiene as opposed to environmental hygiene, about two-thirds of the book deals with the former. After dealing with the general aspects of personal hygiene, the hygienic requirements of special groups, the new-born, the school child, and the elderly are considered. The section dealing with foods and metabolism is up to date and the methods of working out diet values in particular is excellent. Instructions for the control of communicable diseases and parasites are adequate, but the nurse without a good working knowledge of the infectious diseases will get no help from the book for recognizing the symptoms of onset, and may fail therefore to advise precautionary measures at a time when they will be most useful.

The account of ventilation, heating, lighting, sewerage and water supply is clear and concise, and the nurse will acquire from it with ease all the requisite knowledge for 'transforming each home which she visits into as hygienic a state as possible'.

The book is written primarily for nurses taking the general nursing certificate and as the whole bias of training is towards the cure of sickness, the nurse is apt to fail to appreciate the preventive aspect. This little book on the 'science of health and its maintenance' will supply an excellent introduction to the wider aspects of her duties.

There are one or two errors, e.g., in the percentage of CO₂ in air on page 129 and in the law relating to the notification of births on page 197, and the explanation of convection on page 134 is rather difficult to follow, but these are minor defects and do not seriously depreciate the value of an otherwise useful little book.

J. M. O.

OTHER BOOKS RECEIVED.

1. *A Treatise on Birth Control.* By an Eminent Doctor. Published by Mrs. A. Mathews. Contraception Inquiry Office, Kuthiathode, Travancore. 1933.
2. *A Short Review of Some Modern Problems in Public Health Work.* By S. N. Consul, B.Sc., M.B., B.S., D.P.H. (Lond.). Published by the Author, Jaipur State.
3. *The Clinical Aspect of Chronic Poisoning by Aluminium and its Alloys.* By L. Spira, M.D. London: John Bale, Sons and Danielsson, Ltd. Price, 2s. 6d.
4. *Le Nystagmus Vestibulaire et les Reactions de mouvements.* By R. Clauue. Published by Editions Medicales Norbert Maloine, Paris.
5. *Medical Research Council Epidemiological Study of Scarlet Fever in England and Wales since 1900.* By H. M. Woods. London: Published by His Majesty's Stationery Office. 1933. Price, 1s. 3d.

Correspondence

THE TREATMENT OF ACNE

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—With reference to Dr. P. H. Bhatt's letter (published in the May issue of your journal, page 302), asking for suggestions in treating a case of acne vulgaris, I would like him to try about twenty injections (intravenous) of calcium chloride or calcium gluconate (5 to 10 c.cm. of 10 per cent solution), in addition to local treatment recommended by Lieut.-Col. Acton.

It is stated that injections of calcium chloride cause disappearance of almost all papules and pustules in some cases, and marked improvement in many of them with diminution of the oiliness of the skin and even the disappearance of comedones.

Yours, etc.,
S. R. INGLE,
Medical Officer.

MIRAJGAON, AHMEDNAGAR DISTRICT,
13th June, 1933.

THE INTERNATIONAL POPULATION UNION

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I have been trying for some time to organize a National Committee of the International Population Union in India. I think population problems are of such importance in India that an organization of this kind can do very useful work. I succeeded in getting the Indian Economic Association interested in this

question and at their last annual meeting they appointed a committee consisting of Dr. Radhakamal Mukerji of the Lucknow University and myself to report on the feasibility of starting a National Committee in India and to suggest the lines on which it should be organized. A committee of this kind cannot, of course, be confined to economists alone. I shall, therefore, consider it a favour if you would bring this proposal to the notice of medical men through your *Gazette* and ask those interested in this matter to communicate with me.

My idea at present is that the national organization should be an independent unit but should work in close co-operation with the other learned societies of India, like the Indian Science Congress and the Indian Economic Association. I do not know if there is a medical association of this kind but if there is its co-operation will be welcome.

As regards the International Population Union, they are quite willing to recognize a national association. I am going to England and I hope to obtain from them the conditions on which affiliation as a national unit in the International Union would be given to the Indian Association. The terms will be communicated to persons interested in this proposal after my return at the end of September.

Yours, etc.,
DR. B. N. KAUL,
Chairman, Economics Department.

ALIGARH MUSLIM UNIVERSITY,
ALIGARH, U. P.,
3rd June, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL C. A. SPRAWSON, C.I.E., V.H.S., is appointed Honorary Physician to The King, *vice* Colonel W. H. Leonard (retired), 12th February, 1933.

Colonel H. R. Nutt, V.H.S., Inspector-General of Civil Hospitals, United Provinces, was appointed to officiate as Surgeon-General with the Government of Bombay, with effect from the 29th March, 1933.

Lieutenant-Colonel M. S. Irani, Superintendent of Matheran, to officiate as Civil Surgeon, Nasik, in addition to his own duties, *vice* Mr. A. D'Silva.

Lieutenant-Colonel R. G. G. Croly, Professor of Surgery, Medical College, Madras, is appointed to officiate as Surgeon-General with the Government of Madras, *vice* Major-General C. A. Sprawson, C.I.E., V.H.S., granted leave out of India.

The services of Major H. J. Rice, M.C., and Captain T. J. Davidson are placed temporarily at the disposal of the Government of Burma, with effect from the date on which they assume charge of their duties.

Major B. Z. Shah on his return from leave to officiate as Civil Surgeon, Dharwar, with attached duties, *vice* Mr. D. S. Dhavle.

The services of Captain R. D. Alexander are placed temporarily at the disposal of the Government of Madras, with effect from the 3rd April, 1933.

The services of Captain A. Tait are placed at the disposal of the Government of Bombay, with effect from the afternoon of 12th June, 1933, for appointment as officiating Superintendent, Central Mental Hospital, Yeravda.

The services of Captains F. E. B. Manning and W. Lawie are placed temporarily at the disposal of the Government of the United Provinces, with effect from the date on which they assume charge of their duties.

To be Captain (on probation)

B. N. Khan, 24th April, 1933.

To be Lieutenants (on probation)

Said Ahmad.

C. C. Kapila.

W. M. E. Anderson, 24th April, 1933, and remains seconded.

R. D. Scriven, 28th April, 1933.

LEAVE

Major-General C. A. Sprawson, C.I.E., V.H.S., Surgeon-General with the Government of Madras, is granted leave out of India on average pay for 2 months and 2 days combined with leave on half average pay for 19 days, with effect from the 14th July, 1933.

Lieutenant-Colonel A. D. Stewart, Director, All-India Institute of Hygiene and Public Health, Calcutta, is granted leave on average pay for 2 months, with effect from the 15th July, 1933. He was permitted to prefix the holidays on 14th and 15th April and the Institute vacation from the 16th April to the 14th July to the leave.

Major E. C. A. Smith, Superintendent, Central Mental Hospital, Yeravda, is granted leave on average pay for 8 months followed by leave on half average pay for 4 months, with effect from 6th June, 1933, or subsequent date of relief.

PROMOTIONS

The provisional promotion to the rank of Captain of the undermentioned I.M.S. officers is confirmed, subject to His Majesty's approval:—

A. M. Fraser.	G. K. Graham.
M. H. Shah.	A. W. West.
J. R. Dogra.	A. B. Guild.
S. Narain.	Dev Datt.
M. G. Saincher.	R. T. Hicks.
B. L. Taneja.	

Lieutenants to be Captains

F. M. Sewell. Dated 7th March, 1930.

W. Fleming. Dated 22nd May, 1933. (After forfeiting 3 months' service for promotion.)

Lieutenants (on prob.) to be Captains (on prob.)

S. W. H. Askari. Dated 3rd January, 1933.

D. P. Nath. Dated 21st May, 1933.

Captain E. G. Michelson forfeits 12 months' service for purposes of promotion. Dated 4th January, 1933.

Captain G. J. Smith forfeits 6 months' service for purposes of promotion. Dated 24th September, 1932.

Lieutenant W. Fleming forfeits 3 months' service for purposes of promotion. Dated 31st July, 1931.

RETIREMENTS

Lieutenant-Colonel W. E. Brierley retires, 8th April, 1933.

Major M. Murphy, M.C., retires, 22nd May, 1933.

Notes

THE 42ND CHEMISTS' EXHIBITION, LONDON

THIS Exhibition will be held this year from 25th to 29th September in the New Hall of the Royal Horticultural Society, Westminster, S.W. It has been organized on much the same lines as in previous years, and will give the chemist an opportunity of seeing all the newest appliances and drugs that he deals with in his profession. The management, as hitherto, is pleased to welcome visitors from the Dominions and Colonies, and such gentlemen will be admitted on presentation of business cards.

ATEBRIN-PLASMOQUINE

MESSRS. HAVERO Trading Company, Ltd., the sole importers of the above well-known antimalarial drugs, are glad to announce that on account of the steadily increasing demand for plasmoquine, they have been able to reduce the prices of the current trade packings of all plasmoquine preparations by 25 to 30 per cent.

The reduction of Atebrin prices is, however, less striking as the company continues to pay a 30 per cent customs duty for this drug.

A list showing the new prices can be had on request.

THE RISKS OF LIQUID MILK

(Reprinted from the *Medical World*, 27th March, 1931)

IN these days when lactation is fast becoming a lost art the most responsible task facing the general practitioner is the due selection of an artificial food; if he gives mistaken advice he is certain to be reviled for every juvenile complaint that maternal solicitude ascribes to its use for many a day after. Moreover, when the doctor adds to her toilsome duties by stopping her simple drafts on the fount of Nature, the mother must exchange her milk, warm, sterile and amphoteric, for an elaborate concoction based upon cow's milk, of uncertain source and even if carrying an official guarantee probably defiled in domestic storage unless heated to a degree destructive of nutritive properties.

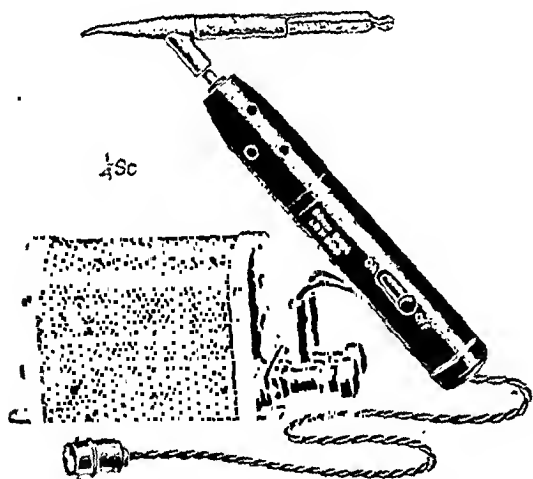
But both the doctor's responsibilities and the mother's toils may be discounted entirely by the use of a simple preparation of standard composition such as the COW & GATE milk food. It is unnecessary to repeat how greatly the composition of milk varies on account of a number of causes: the feeding of the cow, the source of the supply, and, above all, its accidental pollutions. Notorious also is the contamination to which it is exposed in the course of distribution—the transfer to household vessels, and even when bottles are supplied, their rapid infection while awaiting refilling. In short, there is no safety in a fluid which is the most admirable culture medium known, and to which no amount of 'grading' ensures its bacterial innocence. With Cow & Gate milk foods the whole picture is changed. Of uniform composition at all times, when reconstituted with pure water only, it represents a super-grade milk free from all impurities.

METRI-CAUTERY FOR INFECTED CORNEAL ULCERS

By A. CHRISTIE REID, M.D.

THE instrument shown in the accompanying figure, made for me by Messrs. Down Bros., is an improvement on the design of Professor Passow, and has proved invaluable, (a) in arresting septic corneal ulcers that have not yet developed hypopyon; (b) in checking the progress of severe hypopyon ulcers and leaving, even in advanced cases, a very moderate scarring, allowing sometimes a most surprising degree of vision.

The point should be heated from the main electric supply till the thermometer registers 70°C.; it should not be applied over 85°C. A gentle stroking of the surface of the ulcer for a few seconds usually suffices. The process may be repeated later if any fresh advance is noted, but then, as a rule, only to the advancing edge.



The instrument has proved in my hands much less damaging than the actual cautery, even at a dull red heat and by the 'approach' method, that is, not touching.

TREATMENT OF TUBERCULOSIS WITH OILY SUSPENSIONS OF GOLD

In a recent communication to the International Tuberculosis Conference at the Hague Drs. F. Dumarest and H. Mollard report as follows:—

'For the last six years we have been occupied in studying the treatment of tuberculosis with gold. During the last eighteen months we have been led to investigate in particular the use of gold compounds suspended in oil. What was the starting point of our trials and what were their first results?

Impressed by the numerous and often serious secondary effects observed by our predecessors in the field of chrysotherapy, we first of all commenced with the administration of minute, almost homeopathic

doses. We believed that the danger of gold salts consisted in their toxic effect on the organism.

We found, however, that the small doses gave us only a very small percentage (12 per cent) of radiologically demonstrable improvement and the secondary complications of the treatment remained frequent. We then experimented with the administration of higher doses, even giving as much as 1 gramme per week. We observed two facts. Firstly, the frequency of improvement in the patients was much increased. The number of cases developing toxic symptoms became neither more nor less numerous.

This study permitted us to draw two conclusions: the higher doses were incomparably more efficacious than the small doses. The secondary complications were independent of the dosage and were rather a sign of intolerance than of intoxication.

The problem, therefore, was to inject as large a dose as possible and at the same time to increase the tolerance of the patient. At this stage, on the advice of our colleague, Dr. Feldt, and by analogy with certain forms of anti-syphilitic therapy, we conceived the idea of preparing oily suspensions of gold.

Theoretically oily suspensions have two advantages over aqueous solutions:

I. *They are better tolerated by the patient* on account of the slow rate of absorption of the medicament, which must cross over two thresholds before reaching the blood, i.e., that of the oil and that of the muscle cells. Not only is it delivered drop by drop into the circulation, but between the time of making the injection and the moment when the last drops enter the organism a period of 4—8 days elapses. The organism is thus provided with a supply of the product which is absorbed very slowly. Thus there is no violent shock and the body gradually becomes accustomed to the preparation.

II. *The action of the suspended substance is prolonged.* The injected material only accomplishes its voyage through the body little by little. When the first particles are being excreted in the urine and the faeces, other particles are still present in the muscle at the site of injection. The organism thus remains under the influence of the product as long as this metabolic process lasts. The action of the medicament is continuous instead of transitory.

On this theoretical basis we prepared a 20 per cent solution of 'Solganal-B' (aurothioglucose) in almond oil, which we injected three times a week in almost constant doses. At first we gave three injections of 0.2 gramme of the gold compound, then three injections of 0.3 gramme, after which we continued to inject 0.4 gramme till the end of the course, i.e., 12 grammes per week until 8—10 grammes in all had been given.

To-day we are able to present the results of these three experiments:—

I. *The method of injecting small doses in aqueous solution* produced a radiologically demonstrable improvement in 12 per cent of cases, and secondary toxic effects were observed in 60 per cent.

II. *Treatment with higher doses but still in aqueous solution* produced improvement in 52 per cent of cases and slight or severe complications in 60 per cent.

III. *Still larger doses but in oily suspension* produced rapid improvement in 60 per cent of cases and slight secondary symptoms in 39 per cent.

So much for quantitative results. Qualitatively we observed that with oily suspensions the success of treatment was more rapid and more often complete than formerly. More important still, any secondary symptoms observed were slight, transitory and in no case prevented continuation of treatment after a brief interruption.

Further, we would add that many cases who did not tolerate small doses in aqueous solution supported large doses of the oily suspension without any signs of intolerance and with highly beneficial results.

Our experiments, therefore, completely confirmed the theory on which our researches were based. What practical conclusion can we draw from them? This

method, which we have applied personally to a large number of patients, has two chief indications; it increases tolerance and is, therefore, particularly suitable for fragile patients who are highly susceptible to gold, and for patients who tolerate the aqueous solution badly. It enhances the action of the gold compound and is thus especially suitable for patients who are resistant to the ordinary forms of gold therapy.

THE BURROUGHS WELLCOME AND CO. EXHIBITS AT THE CHICAGO EXPOSITION

THE exhibits represent the most recent steps towards ideal therapeutic, dietetic and pharmaceutical preparations. The fixed policy of this firm is never to rest upon laurels already gained, but to press forward constantly to a higher standard of attainment. The steady pursuit of this policy has established amongst professional men throughout the world a confidence in the firm's products which is a reward in itself.

Burroughs Wellcome and Co. are the successors to, and sole proprietors of, the business of Brookedon, who originated compressed medicines in the shape of bi-convex discs. They have pioneered the development of compressed medicaments under their trade mark names 'Tabloid' and 'Soloid' by means of specially-devised machinery, invented and produced at great cost and working with the precision of fine watch-work.

By its aid, under the direction of specially-trained chemists and pharmacists of long experience, compressed products of unique accuracy of dosage, perfection of finish and supreme reliability are produced.

By combining research with industry, pioneer preparations of scientific certainty have been produced, which have replaced the uncertain, unreliable pharmaceuticals of former years. Some of the results of scientific research are the production of drugs, such as 'Diginitin' and 'Ernutin', which replace their uncertain predecessors—tincture of digitalis and extract of ergot. Other examples of the firm's pioneer work are exhibited.

Special attention is devoted to the production of fine chemicals and galenicals of outstanding purity and to the preparation of animal and vegetable medicinal substances of definite strength and activity. The Wellcome materia medica farm assists materially in maintaining supplies of medicinal plants of a high standard of quality.

As pioneers in the supply of medical outfits of high quality and compactness for the use of physicians, surgeons, explorers and travellers, Burroughs Wellcome and Co. have a world-wide reputation. The exhibits include historical medical equipments of the most celebrated pioneers of travel. 'Tabloid' equipments are the only medical outfits to have been carried to the North and South Poles by land, sea and air.

Pioneer research

Burroughs Wellcome and Co. have pioneered the introduction of many new and valuable natural medicinal agents, notable amongst which is *Strophanthus Kombé*, the powerful African arrow poison which has proved so valuable in certain heart disorders.

Sir Thomas Fraser, of Edinburgh University, first investigated and demonstrated the properties of *strophanthus* from a comparatively small specimen, and Burroughs Wellcome and Co. immediately took vigorous steps to procure supplies.

Emissaries were sent to collect the small reserves of arrow poison from the rude huts of many Central African warriors. In this way a fair quantity was accumulated, but at a cost of more than £20 per pound.

These earliest supplies were obtained quite regardless of monetary considerations and, notwithstanding the great cost, parcels of this medicinal agent and its preparations were at once distributed, without charge, to leading physicians throughout the world. By this means the therapeutic properties of *strophanthus* were confirmed by investigators in various lands.

In the treatment of leprosy with esters of acids of the chaulmoogric series, 'Moogrol' has been used in leper colonies throughout the world, and was the result of years of patient investigation and clinical trial. The addition of iodine markedly reduces the irritating property of the ethyl esters, and preliminary clinical evidence obtained with iodized 'Moogrol' has confirmed this.

In the dietetic field, 'Dexin' High Dextrin Carbohydrate marks the outcome of researches conducted in the Wellcome Experimental Research Laboratories, New York.

Ergotoxine—an alkaloid of powerful action in contracting the blood vessels, and isolated owing to the initiative of Burroughs Wellcome and Co. 'Ernutin' is a clear solution presenting ergotoxine—together with 'Ergamine' and 'Tyramine'—in definite amount and in a state of chemical purity. 'Ernutin' (Oral) contains 0.033 per cent and 'Hypoloid' 'Ernutin' 0.1 per cent of ergotoxine ethanesulphonate. 'Ergamine' and 'Tyramine' are organic bases present in ergot.

Alkaline medication

It is difficult to persuade patients to persist in the treatment when sodium bicarbonate and similar alkalis are prescribed in the ordinary way. It is also noted that the psychological effects of such simple prescriptions are not good, and no single alkaline base can secure remineralization of the system, which is often necessary.

'Tabloid' 'Alvesen' solves these difficulties. One in a glass of water produces a very acceptable effervescent draught; the equivalent of 25 doses is contained in a tube; each product presents the alkali bases—sodium, potassium, magnesium and calcium—in precise amounts.

Iron

Because of its hæmatinic value, iron, alone or in combination, is the therapeutic agent most usually employed in conditions of blood deficiency. Iron is conveniently prescribed in the form of Bland Pill.

The therapeutic value of Bland Pill depends upon the presence of iron carbonate in the ferrous state, but in ordinary forms of Bland Pill there is great danger that this ferrous carbonate will be more or less oxidized to the irritating and astringent ferric salt.

The problem of securing the certain administration of ferrous carbonate in an unoxidized condition has been solved by the introduction of 'Tabloid' Bland Pill.

In this product the precise proportions of ferrous sulphate and alkaline carbonate are intimately associated in such a manner that interaction is prevented until the product is administered.

In the stomach, however, the interaction takes place and ferrous carbonate is formed. This fact is sufficient to account for the great superiority of the 'Tabloid' product. It is perfectly stable and permanent until it comes into contact with the gastric secretion.

Ephedra—Ma Huang

Ephedra—known to the Chinese as Ma Huang—is the source of one of the latest additions to our materia medica—the alkaloid ephedrine. Investigation proves that there is great variation in the ephedrine content of different species of ephedra, and that some are practically devoid of activity.

Ephedrine hydrochloride is prepared at the Wellcome Chemical Works, Dartford, Kent (Eng.), elaborate precautions being taken to secure purity, particularly in regard to freedom from pseudo-ephedrine and other subsidiary alkaloids, of which *l*-methyl-ephedrine and *nor-d-ψ*-ephedrine were discovered in Ma Huang by Burroughs Wellcome and Co. Standardization by chemical means ensures uniformity of composition and therapeutic activity.

CAPROKOL

ALTHOUGH it is only a few years since Caprokol was issued, its administration in cases of diseases of the urinary tract has been followed by such striking results that within this comparatively short time its use in the treatment of such diseases has become world-wide.

Caprokol possesses also other properties which are of special value in a urinary antiseptic. For instance, it is chemically stable, non-toxic, non-irritating, analgesic, rapidly bactericidal in high dilution, highly penetrating, active in the presence of organic matter, and free from objectionable odour.

The advantages of these properties in an orally-administered urinary antiseptic are obvious; particularly so is the remarkable fact that such a powerful antiseptic is non-toxic and non-irritating to the mucous membrane of the bladder and of the urethra.

To obtain the maximum benefit from Caprokol treatment, therefore, it is necessary to maintain a uniform concentration of Caprokol in the urine, and, at the same time, to avoid any other form of treatment that is calculated to increase the surface-tension of the urine. Both of these conditions can be secured without difficulty. In order to maintain the normal concentration of Caprokol in the urine it is necessary merely to administer the capsules regularly at the rate of 9 to 12 capsules per diem according to the nature of the infection under treatment, avoiding dilution of the urine by an excessive intake of liquids; in the meantime the surface-tension of the urine can be maintained at a minimum if the precaution be taken not to administer those substances which are known to increase the surface-tension of liquids in which they are dissolved. Examples of such substances are bicarbonate of soda, nitrates and diuretics generally. In this connection it is important to note that mere dilution with water also increases the surface-tension of urine, apart from the fact that the addition of water increases the dilution of the antiseptic; thus for two very good reasons '*forcing fluids*' as commonly employed in the treatment of diseases of the urinary tract should not be administered simultaneously with Caprokol, as this method of treatment, as well as that of treatment by diuresis, obviously tends to defeat the object of the antiseptic therapy.

If the physician is of the opinion that a specific case is one which needs to be treated by diuresis or with '*forcing fluids*' such treatment should be undertaken before the Caprokol administration is started; in no circumstances should two forms of treatment be undertaken simultaneously. If these precautions are observed the results of Caprokol treatment will be uniformly successful, for there is no condition in which Caprokol is contra-indicated.

It is very important to note that in order to ensure permanently satisfactory results from the administration of Caprokol the treatment should be persistent in all circumstances. It is just as important to continue the treatment in cases where an immediate response is observed as it is in cases where the response is not apparent for some time. In other words, on no account should the treatment be abandoned in the early stages either because of apparent cure or of apparent absence of response.

The administration period obviously depends upon the nature of the infection. For instance, in cases of pyelitis and cystitis due to micrococci such as staphylococci and streptococci with no *B. coli* infection the administration of nine capsules *per diem* generally produces sterile urine within two or three weeks from the start of the treatment. If the infection be due to *B. coli* more persistent treatment is necessary; but, except in very rare cases where the infection is an overwhelming one, even this infection will succumb to Caprokol treatment eventually.

In most *B. coli* infections, however, the usual local treatment is advised at first in order to reduce the number of organisms in the early stages. When this reduction is accomplished Caprokol can be relied upon

to produce a completely sterile urine. To effect this, it may be necessary to administer as many as twelve capsules a day, and to persist in the treatment for sixty or ninety days or even longer; eventually, however, complete sterility usually will be effected.

GADIL CALCIC WASSERMANN

GADIL CALCIC is a modification of the well-known remedy 'Gadil' prepared by the Wassermann Laboratories; it is said to be a combination of organic salts of calcium, synthetic guaiacol, menthol, eucalyptol, lecithin, the vehicle being cod-liver oil. It is indicated in the treatment of all tuberculous forms, pulmonary, osseous, articular and intestinal. The ampoules supplied are for hypodermic use in 1, 2 and 5 cubic centimetres.

Another preparation of the same firm is *Ca Wassermann* which is a recalcifying agent, having a strong allaying action in hypervagotonia; its composition is as follows:—

Calcium gluconate	4 per cent.
Calcium pyruvic	4 " "
Calcium lactate	4 " "

It is advocated in the treatment of tuberculosis, pneumothorax, rickets, osteomalacia, fractures of bones, serious hæmorrhages and kindred ills. It is supplied in 2-, 5- and 10-cubic-centimetre ampoules for intravenous or intramuscular use, and can also be had in granule form. Messrs. Ezra Brothers, Rustom Buildings, Churchgate Street, Fort, Bombay, are the distributors in India.

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Original Articles

OBSERVATIONS ON AN UNUSUAL CASE OF ACUTE HÆMORRHAGIC PURPURA

By E. S. PHIPSON, D.S.O., M.D., M.R.C.P.
LIEUTENANT-COLONEL, I.M.S.

Medical Officer in Charge, European General Hospital,
Aden

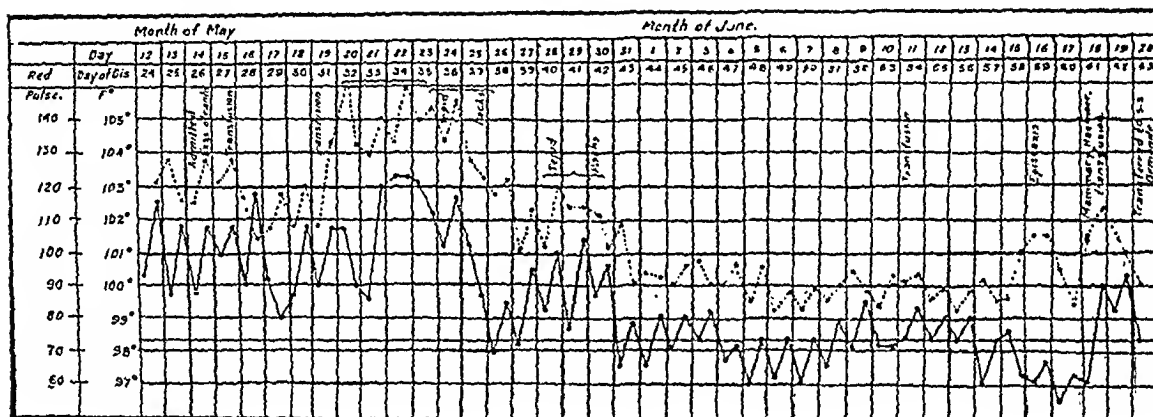
THE purpuras form a peculiar disease-group, the ultimate nature of which is very obscure. As a symptomatic manifestation purpura is associated with a wide range of diseases, many of which are completely dissimilar in character, such, for example, as syringo-myelia, chronic nephritis and smallpox, which have no single feature in common except their occasional association with capillary permeability.

In its primary or idiopathic manifestation, purpura is even more mysterious; its ætiology

disembarked from the s.s. *Otranto* on 14th May, 1933, and admitted to the European General Hospital, Aden, suffering from acute hæmorrhagic purpura.

Previous history.—The patient was an only child, and had lived all her life in the Catanian province of Sicily, in a village remote from the larger towns. Her previous health had been perfect and there was no hæmophilic or similar taint in the family. Menstruation began at the age of eleven, which is quite usual in Sicily, and it proceeded normally. Temperamentally she was very excitable and impulsive, very quick to anger, and ready to quarrel and even fight on a slender pretext. At other times, when nothing occurred to irritate her, she was of a bright and happy disposition. Before leaving Italy she had had a love affair, probably not of a serious character, but unknown to her mother. Her previous history, in so far as it indicates any abnormality, suggests, if not an actually neurotic disposition, at least a temperament less subject than usual to normal inhibitions.

History of present illness.—The patient had completed a normal menstrual period on 15th April, 1933. A few days later she was the horrified witness of a serious motor accident, which gave her a severe nervous shock, and she at once began to menstruate again, and developed what, from her mother's description, was evidently a petechial rash and numerous ecchymoses on



is, it would seem, completely unknown, its essential pathology has so far eluded attempts at elucidation, and its treatment is necessarily to a great extent empirical or symptomatic. Of the primary purpuras, the most remarkable is the acute hemorrhagic type and there are few diseases more striking in character and more dramatic in their developments, and few, fortunately, in which the physician can so safely rely on the *vis medicatrix naturæ*. Of this the most convincing proof is that, despite the absence of any agreed therapeutic rationale, the case-mortality, in any considerable series, is by no means high, and complete eventual recovery is the rule.

The following case is recorded in more detail than usual as it illustrates some of the rarer features of this remarkable disease and emphasizes one point on which all authorities are in agreement: the possibility of recovery in an apparently desperate case:

DESCRIPTION OF THE CASE

The patient, a Sicilian girl of the emigrant class, travelling with her mother from Italy to Australia, was

the limbs and trunk, and later some degree of epistaxis. She consulted a doctor locally who advised certain injections, but, in the preoccupation of the impending voyage to Australia, his advice appears to have been neglected.

The mother and daughter embarked at Naples on the s.s. *Otranto* on 6th May.

For the first four days of the voyage, the epistaxis was troublesome, but she did not seek medical advice until 10th May, when she came under the care of the ship's surgeon, Dr. B. Muir, and, in particular, of his junior colleague, Dr. R. G. Champion de Crespigny, to whom I am indebted for the notes of the case whilst the patient was on board. On 11th May, the epistaxis was severe and was followed by very extensive hæmatemesis (possibly due to swallowed blood). The condition was met by plugging the nares, the injection of horse-serum in the form of antistreptococcic serum, and by subcutaneous salines, with morphia as required. At about this time vaginal bleeding reappeared, and the patient complained of abdominal pain and headache. The temperature varied between 100° and 102°F., and the pulse was fairly steady at about 120. For the next three days her condition gradually deteriorated, and on the ship's arrival at Aden, I was consulted with a view to her disembarkation for further treatment on shore, and she was admitted to the European General Hospital on 14th May.

Condition on admission.—The patient was a girl of medium stature, robust build, and full sexual

development. Her age appeared to be seventeen or eighteen, but her actual age was fourteen. Her breasts were enlarged and full, so much so, that at first sight they suggested lactation, but although the areolæ were enlarged and tumid, the nipples were retracted and inconspicuous. The significance of this became apparent later. Her skin had to a marked degree the waxy pallor of severe secondary anæmia and there was a fine petechial rash sparsely distributed on the skin of the neck and trunk. There were fairly numerous ecchymoses on the limbs and buttocks and below each breast, perhaps a dozen in all, each about two or three inches in diameter, rather faint in colour, and apparently deep-seated in origin. Epistaxis and vaginal bleeding were in evidence and there was a well-marked internal strabismus, alternating in type, but it is doubtful whether the last-named was of recent origin.

Progress of the case.—The symptoms observed on board ship continued to increase in severity. She was given an immediate injection of 30 c.cm. of horse-serum, and six-hourly injections of 4 c.cm. of hæmoplastin (P. D. & Co.) were ordered and arrangements initiated for blood-transfusion.*

Her diet consisted of iced citrated milk and glucose lemonade and 10 per cent glucose in saline per rectum. The following day, 100 c.cm. of citrated blood was transfused, resulting in an immediate and encouraging improvement in the patient's condition; but this, unfortunately, was short-lived and the state of the patient rapidly went from bad to worse. Four days later another transfusion of the same amount was given but it seemed powerless to effect the course of the disease, and by 20th May the condition of the patient was desperate, and she appeared to be moribund.

For the next four days, the girl's condition was pitiable indeed; she lay in a state of extreme bodily weakness, her voice sunk to a whisper, her features pinched and drawn, and with the dusky circum-oral shadow which so often heralds approaching dissolution; almost blind from multiple hæmorrhages in the retinae of both eyes, uncontrollable bleeding proceeding from the nasopharynx, and continual oozing from the gums, mucous membrane of the mouth, palate and tongue; there were frequent hæmatemeses, and rectal incontinence with the continual passage of melæna with occasional gushes of altered blood in quantities which seemed inconsistent with the possibility of survival; continual bleeding in varying amount from the vagina, probably of uterine origin, and enlargement and tumidity of the labia minora, apparently due to the effusion of blood within their substance. The pulse was either hardly perceptible, or of a feeble running quality, almost uncountable, in the neighbourhood of 140 or 150. The temperature varied between 101° and 103°F. with a skin somewhat dry and harsh. The urine contained a trace of albumin but there was no indication of bleeding in any part of the urinary tract.

At this point, when the morbid processes were at their height and survival seemed hardly possible, an observation was made which gave an indication for treatment. This was that the patient was suffering from a profound degree of ketosis, the urine giving the immediate deep purple colour-reaction with Rothera's nitro-prusside test; this is rarely met with except in severe cases of

toxæmia of pregnancy and in acute yellow atrophy of the liver. The patient was promptly put on alkaline carbonates by the mouth in large doses, which fortunately she was able to retain fairly well.

About the same time an effort was made to improve the cardiac condition, although the temperature was not very high, by the old-fashioned method of tepid packs, frequently repeated. The effect on the patient's general condition from these two lines of treatment, particularly the latter, exceeded all expectations and within twenty-four hours all the symptoms showed a perceptible improvement. The pulse became slower and steadier, the pyrexia began to abate and never again attained the same height; the bleeding appeared to be less, and the patient's mental condition was noticeably brighter. It was evidently the turning point in the illness, and thenceforward the patient began an uninterrupted progress towards recovery from the attack. The bleeding gradually stopped and all other symptoms cleared up one by one; and the ketosis diminished and finally disappeared after some days.

The phase of recovery.—From the 24th May onwards, the patient's condition steadily improved, as will be seen from the chart. She was put on hæmatinics in the form of cacodylates of iron and strychnine hypodermically, and liquid liver-extract and colloidal iron by the mouth. Her appetite and digestive power soon returned. By 11th June, her appetite was voracious, and it was difficult to keep her food-intake within reasonable limits. The skin lost its waxy pallor, the features filled out again, and the lips and mucous membranes regained a portion of their normal colour. Visual acuity, which at the height of the attack was almost nil, was partially regained, up to six-eighths.

But in one respect the patient made no progress whatever. Her blood-pressure remained consistently low with a systolic pressure in the neighbourhood of 90 mm. of Hg. and the diastolic pressure of about 45 mm. The result was that any attempt to raise her from the recumbent posture, although keenly desired by the patient herself, led to the development of syncopal symptoms and had to be abandoned. A third blood transfusion was then carried out, but although it improved the general condition somewhat, it had no effect whatever on the blood-pressure. It appeared as if there was a suprarenal deficiency, possibly due to cortical hæmorrhages in the gland-substance, similar to those recorded in the fatal purpura of young infants. On this supposition, an attempt was made to remedy the defect by the cautious administration of adrenalin. This to some extent produced the desired effect. The blood-pressure could be maintained at about 110 mm. (the systolic normal for European girls of a similar age being, as ascertained from a number of observations, 115 mm. during the hot weather in Aden), but the adrenalin injections were painful and had to be abandoned. An affect was then made to bring about a similar rise in blood-pressure by the oral administration of ephedrine hydrochloride, but with indifferent success. In view of the very trying climatic conditions at that time of the year in Aden, it was then decided that no further improvement was likely to be effected in the patient's condition as long as she remained in Aden, and that she was to be sent back as soon as possible to her home in Sicily. This decision was welcomed with delight by the patient and her excitement at the prospect of the voyage home after five weeks' incarceration in hospital may have had some bearing on what followed.

Three days before she was due to leave Aden on the homeward voyage, she developed a slight return of hæmorrhagic symptoms. There was a slight oozing from the gums, with petechial maculæ inside the mouth and lips. This was followed by a slight epistaxis. This development did not occasion any particular anxiety as slight relapses are frequent in cases of purpura, but as a measure of precaution, an injection of hæmostatic serum was ordered and the fourth transfusion decided

*The supply of blood from civilian sources proved to be a difficulty. There was no lack of volunteers, but unfortunately there were no grouping sera in Aden at the time. The difficulty was finally resolved through the admirable medical organization of the Royal Air Force, by which the blood-grouping of certain airmen in each command is known and recorded, and through the good offices of my colleagues, Wing-Commander F. N. B. Smartt, R.A.F.M.S., Principal Medical Officer of the Aden Command, and, in particular, Squadron-Leader J. K. R. Landells, F.R.C.S. (Edin.), R.A.F.M.S., who produced a willing 'universal donor' and carried out the transfusions for me on four occasions. To both these officers I tender my grateful acknowledgments.

on. The following day the oozing and epistaxis had stopped.

During the process of recovery, the girl's breasts had become very much smaller and had assumed what one would judge to be the size and contour normal for a well-developed girl. On the 18th June, at about 10 A.M. the left breast began to swell rapidly, so rapidly that the moment-to-moment increase in size was almost perceptible to the eye. This continued for two or three hours, when the swelling appeared to reach its maximum. The expansion of the breast took place apparently painlessly, but the patient was not unnaturally frightened at the strange experience. At about 4 P.M. of the same afternoon the right breast began to swell in exactly the same manner, and by 7 P.M. both breasts were equally and symmetrically enlarged to the same massive dimensions, suggestive of lactation, as had been observed on her admission to hospital five weeks previously, and with much the same peculiarity of contour, namely, the enlarged and tumid areola and the retracted and almost imperceptible nipple. The cause of this swelling was, no doubt, hæmorrhage into the peri-glandular tissues of the breast and not into the gland itself. This would explain the tumidity of the areolæ and the retraction of the nipple. It seems therefore highly probable that one of the symptoms of the disease, which occurred either in Sicily or on board ship after leaving Naples, was the gradual and painless hæmorrhage into the areolar tissues of both breasts which passed unnoticed by the patient, or, if noticed, was attributed to natural development. The clue to the cause of the original enlargement was the ecchymoses under each breast observed on admission, but its significance was overlooked at the time, and the cause of their reduction in size was, no doubt, the gradual absorption of the extravasated blood during the period of recovery.

I have recorded this incident in detail, as symmetrical massive hæmorrhage into the breasts is unique in my experience in this or in any other disease. I did not regard this development as being of very serious import, as the patient's condition was otherwise quite satisfactory and the urine showed no sign of ketosis.

The following day the breasts had already begun to diminish in size and on the 20th June, after full consultation with the ship's surgeon, she was embarked as a patient on the *s.s. Ormonde* homeward bound for Naples, in the hope that she would reach Italy without further complications, and that she would have a fair chance of complete recovery in the more salubrious climate of her native Sicily.

Discussion

Very little appears to be known regarding the ætiology of this strange affliction. The most recent view, put forward by Jones and Tocantins (1933), is that purpura hæmorrhagica is a disease of the deficiency type, on the ground that blood-transfusion is the most generally effective line of treatment. These authors comment on its marked seasonal tendency—the highest incidence is said to be in the spring—and state that the disease occurs in persons of 'hæmorrhagic constitution'. The acute phase is precipitated by toxins originating from an acute or chronic infectious process which is active, or by substances which affect capillary permeability. They also believe that many cases occur in persons whose diet is ill-balanced. Examining the case under discussion in the light of these views, there appears to be no evidence of the operation of any of the antecedent conditions referred to with the

exception of the one fact that the attack began in the spring.

It is, on the other hand, possible to discern three separate factors in the present case which, acting singly or together, may stand in ætiological relationship to the actual attack. The first and most obvious is the reaction of a young girl of an excitable and unbalanced type to the severe nervous shock occasioned by witnessing a motor accident. The immediate resumption of the menstrual flow on that occasion, and the rapid subsequent development of the petechial rash and of the ecchymoses may, of course, have been purely fortuitous, but the chances are strongly against such a coincidence. The second factor is the probability of the existence of some profound metabolic disturbance, as evidenced by the very high concentration of ketone bodies in the urine at the height of the attack. The third factor is the possibility of endocrine disharmony. This may have resulted from over-action of the endocrine glands subserving the sexual function. That some such factor may have been at work is suggested by the very complete—one might say precocious—sexual development of the girl, the apparent partial failure of adrenal gland-function after the attack, and the unusually heavy involvement of sex organs in the hæmorrhagic manifestations—that is, the breasts, uterus and vulva.

As regards response to treatment, it must be admitted that the effect of the blood transfusions was disappointing. Except on the first occasion, transfusions had very little apparent effect either on the condition of the patient or on the course of the malady. This was perhaps because they were given with insufficient frequency, but with a single donor it is obvious that there are limits to his complaisance as well as to his capacity. The hæmostatic serum, of which relatively large quantities were given, appeared to have a very limited effect, if any, on the occurrence of hæmorrhage, but a marked effect on the blood after it had left the vessels. The naso-pharyngeal space after epistaxis, for example, was frequently occupied by a thrombus in the form of a cast of quite remarkable firmness and tenacity, which, until it was removed (a by no means easy manoeuvre) caused acute discomfort to the patient. So-called specific treatment, therefore, was not strikingly successful.

With regard to general treatment, there is good reason to believe that the adoption of tepid packing at the critical stage in the attack may have had a decisive effect on the circulatory system which enabled the patient to weather the storm, and I think it unlikely that the patient would have survived if the ketosis, in so profound a degree, had remained undetected and untreated.

However this may be, there is one point on which there can be no room for doubt: that the skilled nursing which the case demanded

and received was the predominant factor in the issue of the case, no doubt by fostering those inherent powers of resistance and of somatic response which together constitute the *vis medicatrix naturæ* of the old-time physicians.

It remains for me to record my indebtedness to my Resident Medical Officer, Assistant-Surgeon E. A. Eates, I.M.D., and to my matron Miss-J. Coulter, and the nursing staff, for their loyal co-operation in a difficult case, made no less difficult by the inability of the patient to speak or understand any language but Italian.

In conclusion I should like to add that the heavy cost of specific treatment in this case was met from a fund generously placed at my disposal recently by my friend Sir Prabhashankar Pattani, K.C.I.E., of Bhavnagar.

REFERENCE

Jones, H. W., and Tocantins, L. (1933). *Journ. Amer. Med. Assoc.*, Vol. C, p. 83.

SOME OBSERVATIONS ON TWO CASES OF DISORDER OF THE LIVER IN INFANCY AND CHILDHOOD*

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THE frequency of cirrhosis of the liver in infancy and childhood in India has been long recognized, but cases of disorder of the liver following a course simulating that of acute necrosis have not been reported very often in this country. Furthermore, the subject of cirrhosis has by no means been exhaustively studied, and a satisfactory explanation of many a feature of this illness is lacking.

Recently we came across two cases—one of acute necrosis in a child aged seven and a half years and the other of cirrhosis of the liver in an infant aged one year—in the Carmichael Hospital for Tropical Diseases. Certain observations were made on these cases, which are the subject-matter of this communication.

Case 1.—N. R. B., a boy, aged 7½ years, was born of healthy parents at full time. He was a resident of Rampurhat in Bengal. There was no history of any previous serious illness, neither was there any history of drug or alcohol administration. He took the usual Bengali diet consisting of rice, vegetables, fish, eggs and milk. His parents, brothers and sisters are healthy. No member of the family has had any disorder of the liver, neither was there any history of syphilis.

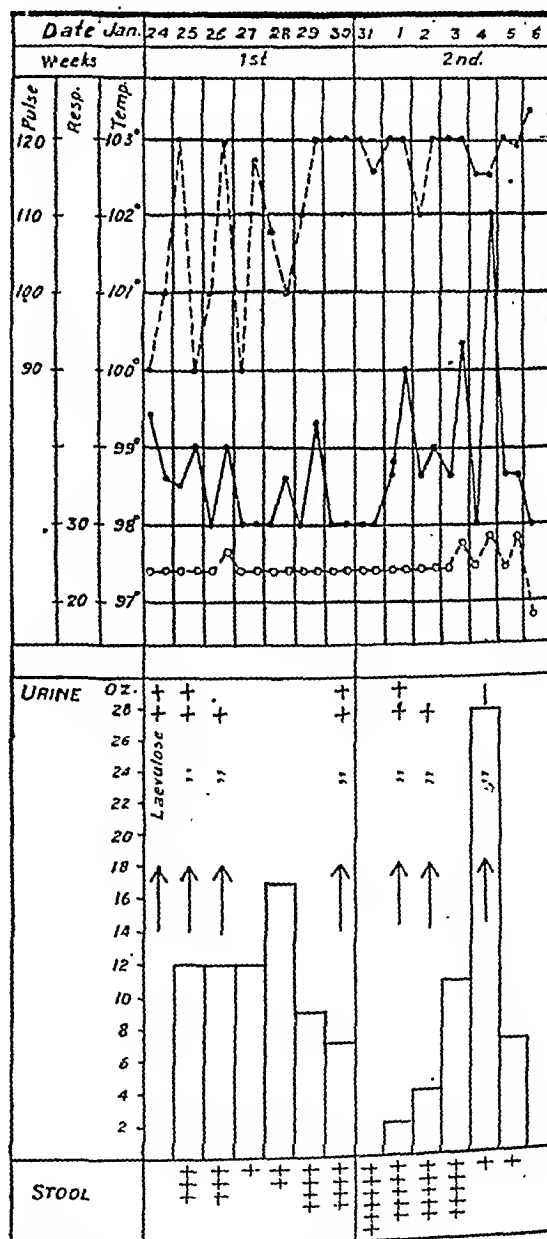
He had frequent, watery motions on the 10th December, 1932; this condition continued for about 10 days, and is reported to have been relieved by the administration of castor-oil emulsion. But he caught a chill and had a swelling of the right auricular region soon after. Following this he had a slow rise of temperature, enlargement of the liver, and jaundice. His condition

improved considerably on a restricted diet containing very little fat, and on receiving three injections of emetine hydrochloride, grains 1/3 each, and a mixture containing salicylates. He was put back on to normal diet as he had no symptoms for about a week. On 5th January, 1933, his condition became suddenly very much worse, as evidenced by the appearance of deep jaundice, swelling of the legs, and rapidly-developing ascites. He was admitted to the hospital in this condition on the 24th January, 1933.

On admission to the hospital the patient was found to be a well-developed boy for his age. There was deep jaundice of the skin and sclera, and œdema of the lower extremities and eyelids. He looked markedly anæmic. The abdomen was protuberant with a considerable amount of ascites. The liver was palpable, hard and smooth, but not tender. The spleen was not palpable. The tongue was clean and moist. There was neither caries of the teeth, nor pyorrhœa alveolaris. The tonsils were septic. The apex of the heart was in the fifth intercostal space at the left mammary line and the precordial dullness extended to this line on the left. There was a thrill and a presystolic murmur at the apex. There was no evidence of disease of respiratory, nervous, or any other system.

Figure 1

Case No. 1.....N.R.B.....Age 7½ years.



Temperature ——— Pulse ——— Respiration ———

* Being a paper read at the British Medical Association (Calcutta branch) on the 21st April, 1933.

Investigations.—Van den Bergh's test gave both 'direct' and 'indirect' positive reactions. Blood examination on the 26th January revealed 45 per cent hæmoglobin, 3,070,000 erythrocytes, and 7,800 leucocytes per cubic millimetre, of which 88 per cent were polymorpho-nuclears, and 12 per cent lymphocytes. Fasting blood-sugar was estimated to be 0.065 milligramme per cent. The Wassermann reaction was negative and the blood was also negative for filaria. Microscopical examination of the stool showed no parasites or ova. Culture of the stool showed *B. pseudo-carolinus*. An examination of the urine done outside on the 16th January showed a trace of sugar. After the administration of 10 grammes of lævulose and 15 grammes of glucose the urine showed lævulose and bile pigment in fair quantities but no glucose; there was a trace of albumin but no casts.

The patient was given no lævulose and was put on a diet consisting of two pints of milk, four ounces of sugar, two ounces of butter, one egg, two oranges and eight ounces of bread daily. Urine examination showed the reaction acid, no glucose, leucin or tyrosin, and no leptospira. The other findings are shown in table I below. For the temperature, pulse rate, respiration and urine reports *vide* figure 1.

TABLE I

Date	Albumin	Lævulose	Bile-pigment	Casts
24-1-33	Nil	++	Nil	Nil
26-1-33	Nil	Nil	Nil	Nil
1-2-33	Trace	++	++	Nil
2-2-33	Trace	+	++	Hyaline granular Do.
4-2-33	..	Nil	++	

Lævulose was tested by polarimeter.

The lævulose-tolerance test was done to determine the efficiency of the liver; the results are tabulated in table II and in figure 1, compared with a control case.

TABLE II (*vide* FIGURE 2)

(Ten grammes of lævulose by mouth)

	Blood sugar, milligramme per cent.
Fasting	0.065
After 45 minutes	0.080
After 90 minutes	0.090
After 135 minutes	0.095

The blood sugar was estimated by the calorimetric method by Dr. J. P. Bose.

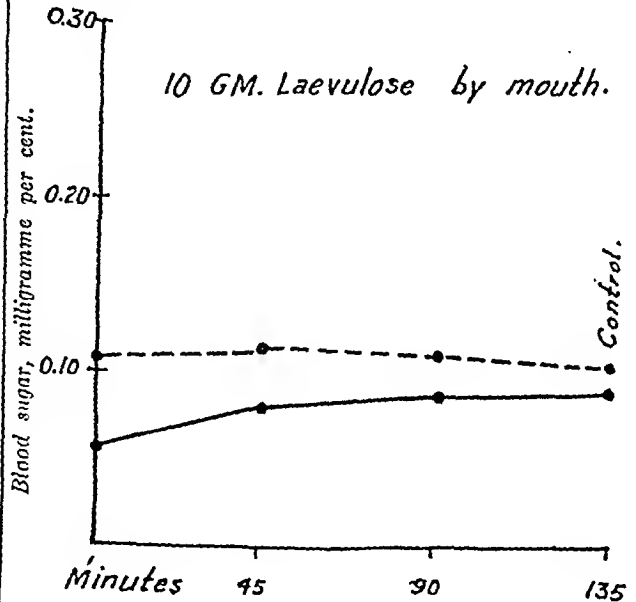
Progress.—The condition of the patient remained steady during the first few days. His appetite improved slightly on being given hypodermic injections of 5 units of insulin coupled with 4 drachms of glucose by mouth, but he did not improve very much. He was then given a fat-free diet consisting of 16 ounces of skimmed milk, 4 ounces of sugar, 3 oranges, one and a half pints of coconut water. The total output of urine diminished very much and on 1st and 3rd of February he was given two intramuscular injections of 0.25 and 0.50 cubic centimetre of novasurol, which increased the output from 6 ounces to as much as 28 ounces in a day, as will be seen from figure 2. His condition gradually became worse and on the 4th February he developed symptoms of loss of vision and hearing, and then passed on to a semi-conscious state. He died on the 6th February. No autopsy was permitted.

Comment

The clinical character of this case resembles very much those described by Wallgren (1930),

Figure 2.

Case No. 1.....N.R.B.....Age 7½ years.



Bergstrand (1930), Williams (1923), Roman (1927) and Morgan and Brown (1927), in which the onset was like that of a benign catarrhal jaundice, then there was slight temporary improvement, followed by the sudden appearance of symptoms pointing to an acute insufficiency of the liver. These authors attempted to establish the relationship between epidemic catarrhal jaundice and toxic necrosis. Many chemicals, such as organic arsenicals, trinitoluene, phosphorus and chineophen, which are known to produce acute necrosis, could be excluded in this case. Both epidemic and sporadic forms of Weil's disease being scattered throughout the country, leptospira infection should be considered as a possible ætiological factor. But the clinical history and course of the disease, and also the absence of leptospira in the centrifugalized deposit of the urine of the patient from the 10th day onwards, provide strong presumptive evidence against its being due to leptospira icterohæmorrhagiæ, although the negative findings might be of questionable value in some instances. Congenital syphilis, typhoid and para-typhoid fever, malaria, tuberculosis, scarlet fever, diphtheria and pertussis can easily be excluded on the basis both of clinical and laboratory findings.

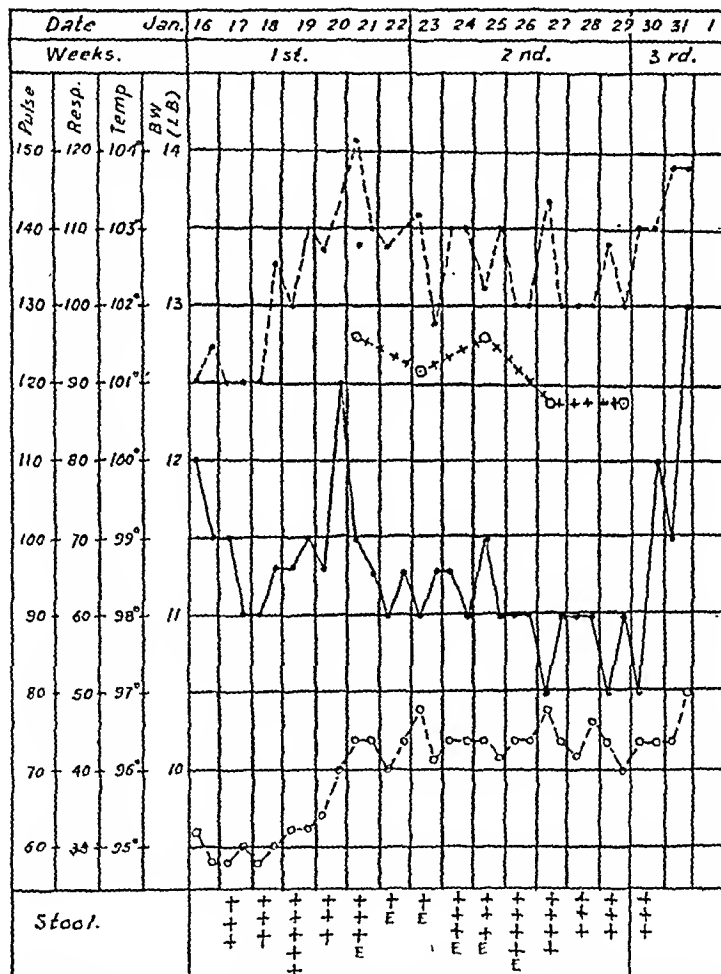
Bergstrand (1930), and Findlay, Dunlop and Brown (1931) have expressed the view that epidemic catarrhal jaundice is probably due to a virus infection, which though pathogenic for man cannot be inoculated into experimental animals. It is possible that acute necrosis of the liver is due to super-added toxæmia in a patient whose liver has been previously damaged by such virus and has not recovered fully after a primary attack. Opie (1910) found acute hepatic necrosis from a combined action of chloroform and *B. coli*. Hurst and Hurst (1928)

produced more marked changes by combining the action of manganese chloride and *B. coli*. Findlay *et al.* (1931) showed that the extent of necrosis is far greater with combined arsaphamin and *B. coli* than with either of them alone. One of us (S. P. B.) observed in a fair number of cases of infantile cirrhosis of the liver, secondary infections with streptococci, *B. coli*, *B. faecalis*, etc., and isolated them from the puncture fluid of the liver and in some instances confirmed these findings by post-mortem examination. Moon (1932) has conclusively demonstrated streptococci in histological specimens of the liver and Bergstrand recovered *Streptococcus viridans* in pure form from the duodenum. Maedonald (1918) reported secondary infection with streptococci in acute necrosis of the liver.

was not recent and was probably connected with the throat infection. The rhythm was regular—90 per minute. There was no extrasystole. The deep jaundice, the irregular rise of temperature, and œdema of the whole body could not be attributed to a cardiac lesion.

A marked disturbance of the functions of the liver is demonstrated by the results of the lævulose-tolerance test. It has been universally accepted that in healthy subjects the blood-sugar level shows hardly any variation after the administration of lævulose, but in disorders of the liver alimentary hyperglycæmia is noticed. It will be seen that in this case the blood-sugar level has increased 35 milligrammes per cent over the initial value which is far from normal. Poynton and Wylie (1926) noted blood-sugar

Fig 3.
Case No. 2. G. I. Age... 1 yr.



Temperature — Pulse - - - - - Respiration o - - - - o Body weight o + + + o

In this case streptococcal infection on the top of a catarrhal jaundice is a reasonable possibility, although a definite proof is difficult to get. There was no jugular pulsation in the neck and the boy suffered no distress whilst lying on his back. There was an enlarged heart with a valvular lesion, but there was no tenderness of the tip of the fingers or toes, no sign of embolism, spleen neither enlarged nor tender, no arteritis of peripheral vessels, no finger clubbing, and no petechiæ noticed. The cardiac lesion

value, which is 'slightly below the average, being 0.053 and 0.056 respectively' in their cases. The initial blood-sugar value in our case, namely 0.065, is definitely below the average in this country. Mann (1927) reported in a recent paper that the complete or even incomplete extirpation of the liver in experimental dogs produces loss of sight and hearing, and coma with concomitant development of hypoglycæmia, ending in death. This could be avoided by repeated administration of sugar.

In our case the symptoms of hypoglycæmia and insulin shock were prevented for a time by the repeated administration of glucose, but after a certain length of time the patient developed loss of sight and hearing, and coma supervened ending in death. This might be due to the sudden disability of a large portion of the liver resembling a partial extirpation, as in experimental animals, because the train of symptoms simulated very much those produced in experimental animals.

In our case the almost constant presence of lævulose in the urine except just before death is remarkable. Then sugar that was reported to be present in the urine on the 16th January was perhaps lævulose, as it was not polarimetrically examined at the time. Lævulose was excreted in the urine both on a mixed diet and on administration of lævulose by mouth, and therefore it could not be considered that it was only a diminished lævulose tolerance, as is seen in functional disorders of the liver, but lævulose diabetes, because lævulose was present even on starvation or when a mixed diet was given. Warkany (1927) reported such an instance of essential lævulosuria in a child suffering from cirrhosis of the liver of tuberculous origin. Barrenschen (1922) also reported a case and collected eleven others from the literature.

It is thus seen that the carbohydrate metabolism is markedly disturbed in this instance. Associated with lævulosuria there is definite hypoglycæmia, which can be reasonably compared with the glycaemic reaction of the diabetic. On oral administration of lævulose, there is a rise of blood-sugar level, which is not seen in normal subjects. This disturbance is undoubtedly due to changes in the liver and perhaps can be explained only on the following assumptions :—

1. Inability of the liver to convert lævulose into dextrose or glycogen.
2. Inability to store glycogen.

The positive van den Bergh reactions, both 'direct' and 'indirect', which suggest obstruction of the bile passages with fair degree of liver damage, and the clinical signs, namely, jaundice, ascites, enlarged liver, etc., all point to gross disorder of the liver, and lævulosuria is another manifestation of this disorder. That the liver was poor in glycogen store is obvious, because the blood-sugar level on fasting was very low.

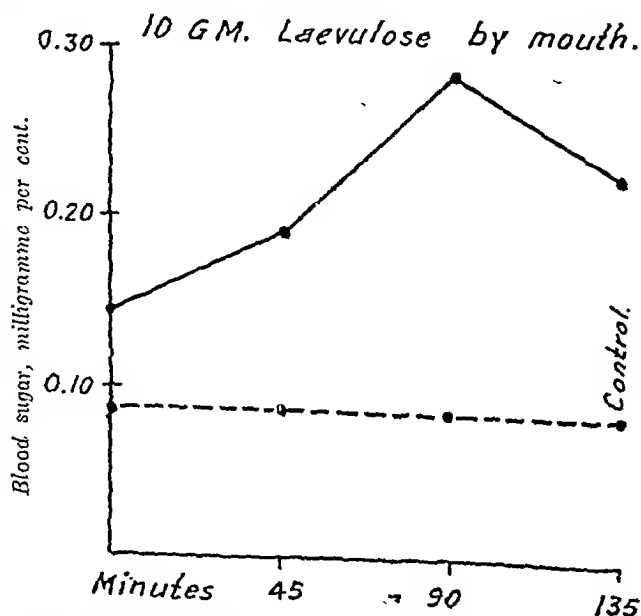
Case 2.—G. I., a boy, aged 12 months, was born of healthy parents at full time. His parents used to live in Madras and came to Calcutta only in November 1932. Both the parents are healthy and the mother has had no miscarriages. There is no history of syphilis, or alcohol. The health of the other children is good. The child had been fed with diluted cow's milk and butter-milk since a few days after birth, and was seldom breast-fed. The only previous illness that he had had was slight fever and cough, and occasional diarrhoea. On the 2nd January, 1933, he had a little cough and, on the 6th, fever. Three days later he is reported to have passed greyish stools and on the 12th February he developed jaundice, which gradually

deepened. On the 16th January he was admitted to the hospital with deep jaundice, ascites and in a very low condition. For the temperature, pulse rate, respiration and body weight *vide* figure 3.

On admission to the hospital the patient was found to be deeply jaundiced and emaciated. He presented an anxious, irritable and anæmic appearance. Muscles and subcutaneous fat were very much reduced and turgor was severe. The skin and conjunctivæ were tinged deep yellow. Veins were dilated and prominent on the chest and abdomen, and showed centripetal distribution. The fontanelle was open and two finger-breadths in width. The child had not cut any teeth. He could not sit, stand, nor speak. His body-weight was 12.8 pounds and height 27 inches. The abdomen was protuberant, its girth being 17.75 inches, with ascites. The liver was enlarged two finger-breadths below the costal margin. It was hard, uniformly smooth and not tender. The spleen was just palpable. The thorax was symmetrical and moved equally on both sides with respiration. Signs of bronchitis were present in both the lungs. There was no evidence of disease of the nervous or any other system.

Investigations.—Van den Bergh's test was strongly positive both for 'direct' and 'indirect' reactions. On examining the blood on the 17th January the erythrocytes amounted to 3,150,000 and leucocytes 36,900 per cubic millimetre of which 83 per cent were polymorphonuclears, 14 per cent lymphocytes, 1 per cent mononuclears and 2 per cent eosinophiles. Hæmoglobin was 50 per cent. The Wassermann reaction was negative. Microscopical examination of the stool revealed nothing except the ova of trichuris and culture of the stool showed *B. pseudo-carolinus*. The fat-content of the stool was found to be 2.26 per cent total fat, of which 1.06 per cent was saponified fat, 1.16 per cent non-saponified fat, 0.62 per cent fatty acid and 0.44 per cent neutral fat. Urine examination showed nothing, but lævulose appeared on the administration of 10 grammes of lævulose by the mouth. On culturing a catheter specimen, *B. pseudo-carolinus*, non-lactose

Figure 4
Case No. 2.....G.I.Age 1 year.



fermenters and some fine colonies of streptococci were notified. The results of the lævulose-tolerance test are given in table III.

Röntgenological examination of the skeletal bones showed no rickets or syphilitic change (*vide* skiagram).

TABLE III (*vide* FIGURE 4)
(Ten grammes of lævulose by mouth)

	Blood sugar, milligramme per cent.
Fasting ..	0.149
After 45 minutes	0.190
After 90 minutes	0.280
After 135 minutes	0.220

Progress.—His condition improved transiently on administration of three drachms of glucose by the mouth, and giving 3 to 7 units of insulin hypodermically daily. About a week after admission he developed constipation and troublesome tympanitis, and died on the 1st February, *i.e.*, within 4 weeks of the onset of the first symptom. The course of the disease is represented graphically in figure 3 and a picture of the patient is seen in figure 5. No autopsy was permitted.

changes of rickets. In figure 6, if the skiagram of the wrist of this case is compared with that of a case of rickets, the difference will be obvious to all. In contra-distinction to the view of Naegeli and his collaborators (1931) who observed leucopenia and characteristic granules in the mononuclears, and also to the Mexican series of cases where leucopenia was observed, we have found leucocytosis in this case as well as in many other similar cases. The course of the disease in this instance was unusually rapid and this is perhaps due to the fact that the patient was debilitated and had been artificially fed from the very beginning. On the basis of clinical and laboratory findings, it is impossible to distinguish this case imported from South India from those seen locally. Strongly positive 'direct' and 'indirect' van den Bergh reactions suggest that there was both obstruction of the bile passages and destruction of the

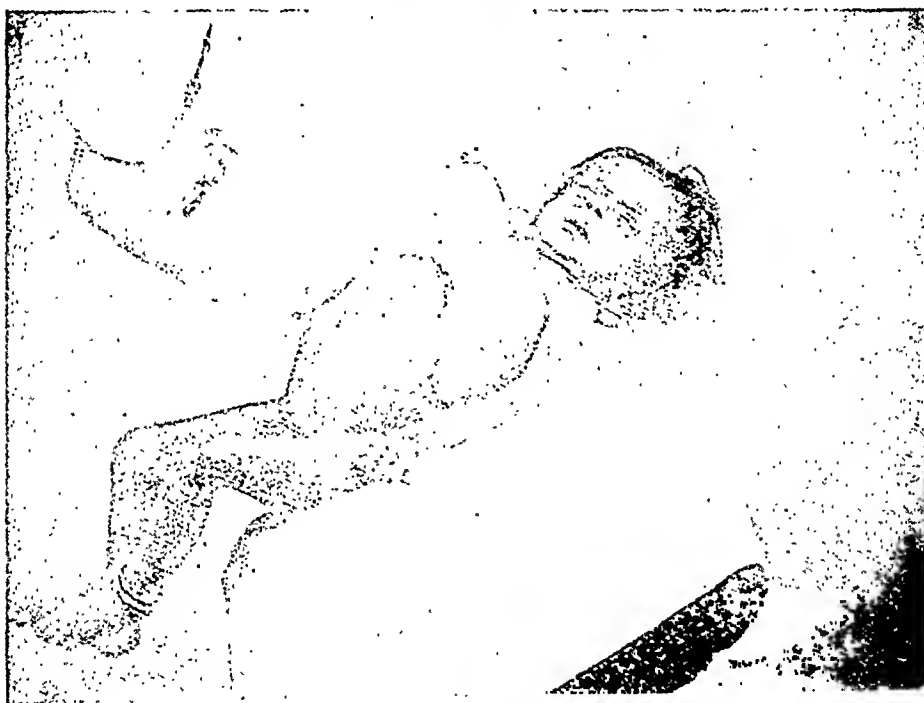


Figure 5

Comment

The diagnosis of this case did not offer much difficulty as almost all the classical signs and symptoms of cirrhosis of the liver, namely, ascites, dilatation of the abdominal veins, jaundice, enlargement of the liver and clay-coloured stools, were present. Poynton and Wyllie (1926) mention that special features related to cirrhosis of the liver in childhood are infantilism, familial incidence and hæmorrhages. Although the familial occurrence and hæmorrhages have not been noticed in this case the signs of infantilism were distinct and unmistakable. Small stature, delayed dentition, open fontanelle, and inability to sit, stand or speak, might be considered as of rickety origin but röntgenological examination of the skeletal bones revealed none of the characteristic

liver cells. There was also definite sign of hepatic inefficiency, as shown by the lævulose-tolerance test. As will be seen from the figure there was very marked deviation of the blood-sugar level, after the administration of 10 grammes lævulose. The rise amounted to as much as 131 milligrammes per cent over the initial blood-sugar level as compared to the rise in normal cases. Hyperglycæmia is also a notable feature which is seen in this case as well as in others of a similar nature.

The search for an explanation of the cirrhosis has given rise to much speculation. Known causes of this disease, syphilis, the alcohol habit, tuberculosis, malaria, kala-azar, congenital malformations of the hepatic system, and acute infections, the rôle of which has been particularly stressed by Osler (1903), could be

definitely excluded. A parasitic type of cirrhosis is known, in which various forms of schistosome are concerned. No parasites or ova were discovered in this case. In many such cases where the origin remains obscure, a



Figure 6
Skiagram

toxin of chemical, metabolic or bacterial origin is perhaps at work. Rolleston (1912) suggested 'a local result of a chronic general toxæmia, with the conveyance of the toxin to the smaller bile ducts by means of the hepatic artery'. Theories differ as to the character of the poison. It is likely that a toxic substance is produced under certain circumstances, which might act as a provocative agent. deRaadt (1930) thought that conditions, which greatly and for a long period increase the conversion of intestinal ammonia into urea by the liver, result in cirrhosis. A diet containing a small amount of nitrogen, such as strictly vegetable diet, would then act in this way. Many difficulties beset the determination of the exact ætiology of the cirrhosis of the liver. At the present stage of our knowledge it is impossible to state anything definite about the nature, origin and pathogenesis of these cases. It must be left to the future for discussion and determination.

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STUDIES ON THE ACTION OF ATEBRIN IN PLASMODIUM INFECTION OF MONKEYS

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NAPIER and Campbell (1932) found that the blood of a monkey imported from the Malay States—*Macaca irus*—contained a protozoal parasite in the red blood corpuscles resembling the malarial parasite. This monkey did not seem to be in any way affected by this infection, which was never intense and which was not always patent, even when a careful and prolonged examination of the blood was made. A few cubic centimetres of the blood of this monkey, in citrated saline injected intravenously into a *Macaca mulatta*, the common monkey occurring in Bengal and many parts of India, transferred the infection to the latter animal.

(Continued from previous column)

REFERENCES

- Barrenschen, H. K. (1922). *Biochem. Zeitschr.*, Vol. CXXVII, p. 222.
 Bergstrand, H. (1930). *Acta Med. Scandinavica*, Supplement, No. 34, p. 331.
 Bergstrand, H. (1930). *Acta Path. et Microbiol. Scandinavica*, Supplement, No. 5, p. 41.
 deRaadt, O. L. E. (1930). *Zeitschr. Klin. Med.*, Vol. CXII, p. 447.
 Findlay, G. M., Dunlop, J. L., and Brown, H. C. (1931). *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXV, p. 7.
 Hurst, E. W., and Hurst, P. E. (1928). *Journ. Path. and Bact.*, Vol. XXXI, p. 303.
 Macdonald, S. (1918). *Brit. Med. Journ.*, Vol. I, p. 76.
 Mann, F. C. (1927). *Medicine*, Vol. VI, p. 419.
 Mann, F. C. (1925). *Journ. Amer. Med. Assoc.*, Vol. LXXXV, p. 1472.
 Masina, N. (1932). *Folia hæmatol.*, Vol. XLVI, p. 335.
 Moon, V. H. (1932). *Arch. Path.*, Vol. XIII, p. 691.
 Morgan, M. T., and Brown, H. C. (1927). *Reports on Public Health and Medical Subjects*. No. 42. London: H. M. Stationery Office.
 Naegeli, O. (1931). *Blutkrankheiten und Blutdiagnostik*, 5th Edn. Berlin: Julius Springer.
 Opie, E. L. (1910). *Journ. Exp. Med.*, Vol. XII, p. 367.
 Osler, W. (1903). *Bull. Johns Hopkins Hosp.*, Vol. XIV, p. 322.
 Poynton, F. J., and Wyllie, W. G. (1926). *Arch. Dis. Child*, Vol. I, p. 1.
 Rolleston, H. (1912). *Diseases of the Liver, Gall-Bladder and Bile-Ducts*. London: Macmillan & Co.
 Roman, B. (1927). *Arch. Path. Lab. Med.*, Vol. IV, p. 399.
 Wallgren, A. (1930). *Acta Ped.*, Vol. IX, Supplement, No. 2, p. 1.
 Warkany, J. (1927). *Zeitschr. Kinder.*, Vol. XLIII, p. 305.
 Williams, H. (1923). *Journ. Amer. Med. Assoc.*, Vol. LXXX, p. 532.

The course of the infection was intense and if allowed to progress, as many as 60 per cent of the red blood cells became infected, and the animal rapidly succumbed.

Knowles and Das Gupta (1932) carried out exhaustive studies in connection with this infection and confirmed the findings of Napier and Campbell. They showed that this parasite occurs as a natural infection in *M. irus*. In this host the infection is scanty, and either spontaneous recovery occurs within a few days or weeks, or a very light infection persists off and on for periods up to seven months or more. No symptoms are produced and morphologically the parasite resembles *P. vivax* of man, and gametocytes are relatively abundant.

Macaca mulatta however is exceedingly susceptible, and the infection invariably proves fatal, usually within a week or less of the first appearance of the parasites. This animal can be infected with an extremely minute dose, e.g., a total inoculation of 16,000 parasites given intravenously or subcutaneously. The fever rises to 106.2°F. (normal temperature being 102° to 103°F.), the animal becomes ill and suffers from profound and progressive anaemia. All phases of the schizogony cycle are seen in the peripheral circulation whilst the terminal phases of infection are of terrific intensity with a parasite count of 3½ million per cubic millimetre. The internal viscera are crammed with parasites and the terminal infection is sometimes accompanied by hæmoglobinuria. Death occurs after a sudden fall of temperature to subnormal.

The infection can also be communicated to some of the other monkeys commonly occurring in India:—(1) in *Macaca radiata*, the parasites are scanty, persist from 5 to 40 days, the count is very low, and spontaneous recovery usually occurs. (2) *Semnopithecus entellus*—the common 'hanuman' monkey of India—is nearly as susceptible as *M. mulatta*; severe infection occurs and progressive anaemia develops leading to a fatal termination. (3) *Hylobates hoolock*—the 'hoolock anthropoid' of Assam—is only slightly susceptible and shows transient infection for a few days unaccompanied by any symptoms.

It has been found that *M. mulatta* and *S. entellus* when infected with this parasite readily react to treatment with anti-malarial drugs, provided of course that the infection has not proceeded beyond a certain limit. Napier and Campbell in their early experiments found that, by giving the infected animal one grain of quinine by the mouth for about a week and then a single dose of 1 to 2 grains every now and then, the infection could be kept in check. Chopra, Mukherji and Campbell (1933) tested the action of some cotarnine derivatives supposed to have anti-malarial properties on *M. mulatta* infected with malaria and obtained results corresponding to those obtained in human beings. Knowles and Das Gupta have shown

that in this species the earlier ring and trophozoite phases bear some morphological resemblance to *P. falciparum* of man, whereas the gametocytes resemble those of *P. malaria*. These workers were successful in transferring this infection from *M. mulatta* to man. After inoculating the blood of infected monkeys into human volunteers they not only produced clinical symptoms such as fever, but found rings and trophozoites in the peripheral blood. Such infected blood inoculated into a *M. mulatta* carried back the infection to these animals after an incubation period of 7 days. This plasmodium, *Plasmodium knowlsi*, Sinton (1933), would thus appear to be more closely related to that occurring in man than plasmodia occurring in birds such as canaries, Java sparrows, etc., and the experimental results should therefore be more readily applicable to man.

In view of what has been said it will be seen that the two species, *M. mulatta* and *S. entellus*, infected with monkey malaria should form a very suitable medium for testing the action of anti-malarial drugs, a number of which have been synthesized lately and some of which have been put on the market. The infection in these monkeys is so intense that it will go on to fatal termination unless the drug is effective. Further, in these animals the course of infection can be watched by carrying out daily counts of the parasites and the treatment can be started at any stage desired. The control of infection by a remedy in such animals is a crucial test of its anti-malarial value as there is no chance of a spontaneous cure especially in the *M. mulatta*. The routine usually followed in this work was to test the drugs on the monkeys infected with malaria first. If beneficial results were produced trials in human patients were carried out. In this paper we give the result of our trial with atebirin.

Experimental

In the following tables are given the results of trials of atebirin in twelve monkeys. The drug was given intravenously and intramuscularly for the reason that in this way a quick and certain action is ensured. The drug given by the mouth in these animals is often kept in the pouch in the neck in which food is stored, and may later be rejected. The introduction of drugs by a stomach tube has been tried but this is liable to produce injury in the region of the pharynx and oesophagus and lead to death from sepsis and pneumonia. This method was therefore not adopted. There is ample evidence however to show that whether the drug is given by the mouth, intramuscularly or intravenously, the results are analogous. The animals under experiment were observed for prolonged periods, in some cases for many months.

The animals used in our experiments were all *Macaca mulatta* because of their ready availability, convenient size and low cost. Besides, spontaneous cure very rarely occurs in

S. entellus, and it practically never occurs in *M. mulatta*. These animals were infected by subcutaneous injection of heavily parasitized blood from *M. mulatta* previously infected. The weight of the animals used varied from 3.2 to 4.7 kilogrammes, except for one large monkey weighing over 5 kilogrammes and a young one less than 2 kilogrammes. In almost every case the treatment was commenced when the infection was very heavy, the maximum count being 1,200,000 parasites per cubic millimetre. Atebrin was given in daily doses of 0.025 gramme in most cases either by the intravenous or intramuscular route. This dose was well tolerated by monkeys of average weight, larger doses producing untoward effects; doses of 0.04 and 0.05 gramme intravenously always proved fatal in 10 to 20 minutes.

In the following tables detailed observations on these animals are summarized:—

No. I, *Macaca mulatta*, 5.3 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood from an animal showing a very heavy infection (counts not done). Incubation period 7 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
26-12-32	?	..	Rings +.
27-12-32	180,000	Atebrin 0.025 gm. i.v.
28-12-32	58,400	Do.
29-12-32	1,600	Do.
30-12-32	Scanty	..	Anisocytosis. Basophilia +.
31-12-32	0
2-1-33	0	..	Anisocytosis +. Normoblasts +.
3-1-33	0
4-1-33	0	..	Scanty pigment-bearing leucocytes.
5-1-33	0
9-1-33	?	..	Rings and schizonts.
10-1-33	508,800	Atebrin 0.025 gm. i.v.	All phases parasites.
11-1-33	440,000	..	The animal is very ill. No injection given. All phases parasites.
12-1-33	Died last night. Heart blood shows a very large number of parasites.

In this animal three doses of atebrin were given intravenously when the parasite count of the peripheral blood was very high. The parasites disappeared after the injections but reappeared 11 days later (9th January, 1933) and rapidly increased in number (10th January, 1933). An intravenous injection of 0.025 gramme was given (10th January, 1933) and next day the number of parasites decreased somewhat but the animal died. It had not been realized that relapse takes place so quickly after atebrin and therefore the drug was not administered earlier. It would however appear that once the parasites increased beyond a certain limit atebrin might not be very effective in checking their growth.

No. II, *Macaca mulatta*, 4.64 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 244,000,000 parasites. Incubation period 7 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
19-12-32	Scanty	..	Rings.
20-12-32	19,200	Atebrin 0.01 gm. in 2 c.cm. of dist. water, i.v.	Rings and mature schizonts.
21-12-32	2,200	Do.
22-12-32	0	Do.
23-12-32	0
24-12-32	?	..	Rings.
30-12-32	?	Atebrin 0.025 gm. i.m.	Rings +, schizonts +.
31-12-32	18,400	..	All phases.
2-1-33	Very scanty	..	Degenerate.
3-1-33	Do.
4-1-33	?	..	Rings. Marked basophilia.
5-1-33	Scanty	..	Rings and schizonts.
9-1-33	0
10-1-33	0
18-2-33	0
27-2-33	?	..	Rings +. Growing trophozoites +.
7-3-33	?	..	Rings.
18-3-33	0
28-3-33	0
18-4-33	0
21-4-33	0
17-7-33	Animal died—post-mortem showed consolidation of both lungs. No parasites in the heart blood.

In this animal atebrin 0.01 gramme was given intravenously for 3 days when the parasite count was not very high. The parasites disappeared for 2 days but reappeared in increased numbers. 0.025 gramme of atebrin was given intravenously (30th December, 1932). The animal showed parasites in the peripheral blood every now and then but the infection appears to have lost its virulence. This animal has been under observation for about seven months.

No. III, *Macaca mulatta*, 2.965 kilogrammes in weight inoculated with 0.35 cubic centimetre of blood containing 168,000,000 parasites (almost all phases). Incubation period 5 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
5-2-33	?	..	Rings +.
6-2-33	810,000	Atebrin 0.025 gm. i.m.	Sexual and asexual.
7-2-33	Very scanty	Do.	Degenerate.
8-2-33	0	Do.
9-2-33	0	Do.
13-2-33	0
18-2-33	0
20-2-33	0
23-2-33	Monkey died. Heart blood shows very numerous parasites.

In this animal atebirin 0.025 gramme was given intramuscularly for 4 consecutive days when the parasite count in the peripheral blood was very high. The blood became free from parasites after 2 injections (8th February, 1933). The monkey suddenly died 15 days later (23rd February, 1933) and blood from the heart showed numerous parasites.

It will thus be seen that monkeys I, II and III, all relapsed after receiving 3 and 4 doses of atebirin both by the intramuscular and intravenous routes. In no. III, no treatment was given as the significance of occurrence of relapses after treatment had not been appreciated.

No. IV, *Macaca mulatta*, 3.565 kilogrammes in weight inoculated with 0.4 cubic centimetre of blood from a heavily infected animal (counts not done). Incubation period 7 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
20-2-33	Scanty	..	Rings.
21-2-33	22,240	Atebrin 0.025 gm.i.m.	Rings, schizonts, gametocytes.
22-2-33	9,820	Do.	Many degenerate.
23-2-33	0	Do.
24-2-33	0	Do.
27-2-33	0
1-3-33	0
4-3-33	0
6-3-33	0
7-3-33	?	..	Rings +.
8-3-33	80,000	Atebrin 0.025 gm.i.m.	Chiefly growing trophozoites.
9-3-33	Scanty	Do.	Degenerate.
13-3-33	Very scanty
18-3-33	0
20-3-33	?	..	Schizonts +.
21-3-33	?	..	Do.
25-3-33	?	..	Schizonts and gametocytes.
28-3-33	?	..	Rings and schizonts +.
29-3-33	Scanty	..	Schizonts.
31-3-33	?	..	Schizonts +.
3-4-33	Scanty	..	Schizonts.
11-4-33	?	..	Do.
18-4-33	?	..	Rings +.
21-4-33	0
27-4-33	0
1-5-33	?	..	Schizonts +.
5-5-33	?	..	Schizonts, rings.
17-7-33	0
22-7-33	0

No. V, *Macaca mulatta*, 3.3 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 11,120,000 parasites (chiefly rings and schizonts and a few gametocytes). Incubation period 8 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
27-2-33	0	..	Rings.
1-3-33	Very scanty	..	Rings.
2-3-33	12,800	Atebrin 0.025 gm.i.v.	Rings and schizonts.
3-3-33	1,600	Do.	Degenerating rings.

No. V, *Macaca mulatta*—concl'd.

Date	Parasite count per c.mm.	Treatment	REMARKS
4-3-33	0	Atebrin 0.025 gm.i.v.
6-3-33	0	Do.
7-3-33	0
9-3-33	0
13-3-33	0
18-3-33	52,240	Atebrin 0.025 gm.i.m.	Chiefly schizonts.
20-3-33	Scanty
21-3-33	0
22-3-33	0
28-3-33	?	..	Rings +, schizonts +.
31-3-33	?	..	Schizonts +.
3-4-33	Scanty	..	Schizonts.
11-4-33	0
18-4-33	Scanty	..	Schizonts.
24-4-33	0
1-5-33	0
5-5-33	0
17-7-33	0
22-7-33	0

This animal has been under observation for five months, 0.025 gramme given intravenously for four days when the parasite count was not high. The parasites disappeared, but reappeared 12 days later (18th March, 1933). A dose of 0.025 gramme of the drug was given and after this the parasites disappeared but reappeared again. Ring forms and schizonts were both seen but the infection appeared to have lost its virulence and did not progress to a fatal termination.

No. VI, *Macaca mulatta*, 3.2 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 42,140,000 parasites (rings and schizonts predominating). Incubation period 7 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
21-3-33	Scanty	..	Schizonts.
22-3-33	?	..	Rings and schizonts +.
23-3-33	520,000	Atebrin 0.025 gm.i.m.	Chiefly rings.
24-3-33	11,480	Do.	Majority degenerating.
25-3-33	6,240	Do.	Degenerating rings and trophozoites.
26-3-33	0	Do.	Marked basophilic demilune cells and a few normoblasts present. 1,820,000 R. B. Cs. per c.mm.
28-3-33	0
31-3-33	0
3-4-33	0	..	R. B. C. 6,240,000 per c.mm.
9-4-33	The animal died and the heart blood showed countless parasites.

This animal was given 0.025 gramme of atebirin intramuscularly on four consecutive days. The parasites disappeared but a fortnight later the animal died from the infection.

No. VII, *Macaca mulatta*, 3.7 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 11,120,000 parasites (chiefly rings, schizonts and a few gametocytes). Incubation period 9 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
2-3-33	?	..	Rings +.
3-3-33	?	..	Rings, growing trophozoites, schizonts +.
4-3-33	124,000	Atebrin 0.025 gm. i.v.	Chiefly rings.
6-3-33	Very scanty	Do.	Degenerating.
7-3-33	0	Do.
8-3-33	0	Do.
9-3-33	0	Do.
13-3-33	0
18-3-33	92,840	Atebrin 0.025 gm. i.m.	Rings.
20-3-33	0
21-3-33	0
22-3-33	?	..	Rings and schizonts +.
28-3-33	?	..	Do.
29-3-33	?	..	Schizonts +.
31-3-33	Scanty	..	Rings.
3-4-33	0
11-4-33	Scanty	..	Rings.
18-4-33	?	..	Do.
21-4-33	Scanty	..	Schizonts.
22-4-33	Scanty	..	Schizonts and rings.
27-4-33	Scanty	..	Schizonts.
1-5-33	0
5-5-33	0
17-7-33	0
22-7-33	0

This animal has been under observation for about four months. Atebrin in doses of 0.025 gramme was given intravenously for five days when the infection was heavy. The parasites disappeared but reappeared nine days later (18th March, 1933) and a further dose of 0.025 gramme was given intramuscularly. After this the parasites disappeared but reappeared later. The infection however seems to have lost its virulence and did not progress to a fatal termination. For the last two months no parasites have been detected, and the animal is still under observation.

No. VIII, *Macaca mulatta*, 4.9 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 210,000,000 parasites (chiefly schizonts). Incubation period 8 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
29-5-33	0
30-5-33	Scanty
31-5-33	14,980	..	Rings and schizonts.
1-6-33	222,800	Atebrin 0.05 gm. i.m.	Chiefly schizonts.
2-6-33	19,200	Do.	Degenerating rings.
3-6-33	0	Do.
5-6-33	0	Do.
6-6-33	0	Do.
7-6-33	0
8-6-33	0
10-6-33	0
26-6-33	Found dead.

This animal was given 0.05 gramme of atebtrin intramuscularly on five consecutive days. The parasites disappeared but a fortnight later the monkey was found dead in its cage, probably of a relapse. Unfortunately the animal was decomposed on account of the heat and the blood could not be examined.

No. IX, *Macaca mulatta*, 4.4 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood containing 7,490,000 parasites (chiefly rings and schizonts). Incubation period 5 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
5-6-33	Very scanty	..	Rings.
6-6-33	Scanty
7-6-33	30,800	..	Chiefly schizonts.
8-6-33	240,000	..	Chiefly growing trophozoites.
9-6-33	1,200,000	Atebrin 0.05 gm. i.m.	Early schizonts.
10-6-33	184,000	Do.	Degenerating rings and growing trophozoites. Pigmented hyalines ++++. Monkey very anemic.
12-6-33	0	Do.	Normoblasts +.
13-6-33	0	Do.	Basophilia +.
14-6-33	0	Do.	Normoblasts +.
27-6-33	72,800	Do.
30-6-33	0	..	Rings and schizonts.
1-7-33	0
3-7-33	0
10-7-33	Scanty	..	Schizonts and gametocytes.
11-7-33	?	..	Schizonts, gametocytes and rings.
12-7-33	0
17-7-33	?	..	Rings +.
22-7-33	0

This animal was given 0.05 gramme of atebtrin intramuscularly for five days and the parasites disappeared from the peripheral blood. Thirteen days after the last dose the parasites reappeared and another dose of 0.05 gramme of the drug was given intramuscularly (27th June, 1933). The parasites reappeared a fortnight later (10th July, 1933) and after persisting in the peripheral blood for some time they disappeared spontaneously. The animal is still under observation.

No. X, *Macaca mulatta*, 6.1 kilogrammes in weight inoculated with 0.5 cubic centimetre of blood from a heavily parasitized monkey. Incubation period 7 days.

Date	Parasite count per c.mm.	Treatment	REMARKS
7-7-33	?	..	Rings and growing trophozoites present.
8-7-33	38,240	..	All phases.
9-7-33	72,840	..	Do.
10-7-33	102,240	..	Do.
11-7-33	882,000	Atebrin 0.05 gm. i.m.	Chiefly schizonts. Pigmented mononuclears +++.

No. X, *Macaca mulatta*—concl'd.

Date	Parasite count per c.mm.	Treatment	REMARKS
12-7-33	Very scanty	Atebrin 0.05 gm. i.m.	Degenerating. Animal very anæmic, 2,180,000 R. B. Cs. per c.mm.
13-7-33	0	Do.	Scanty pigmented leucocytes. Marked anisocytosis, basophilia.
14-7-33	0	Do.
17-7-33	0	Do.	Passed diarrhoeic stool.
21-7-33	0	..	No abnormal cells. 5,840,000 R. B. Cs. per c.mm.
26-7-33	?	..	A few rings and schizonts.

This animal was given 0.05 gramme of atebrin intramuscularly on five days.

Nos. XI and XII died during intravenous injections of 0.05 gramme of atebrin.

Summary and discussion

The above results of these preliminary experiments regarding the action of atebrin on a small series of *M. mulatta* infected with *Plasmodium knowlsi* brings out certain interesting and important points with regard to the action of this drug. It has therefore been considered advisable to publish our findings. It is fully realized, however, that the series is too small upon which to draw any general conclusions and further work to elucidate various problems which have arisen in this connection is in progress.

Destructive action on the plasmodium.—The destructive action of atebrin on this plasmodium would appear to be exceptionally powerful. Usually two doses of 0.025 gramme each given either intramuscularly or intravenously are sufficient to control a very heavy infection which may amount to a million parasites per c.mm. The drug equally effects both the schizogony and the gametogony of this plasmodium and all phases of the parasite disappear rapidly from the peripheral circulation under its action. Even after a single dose, signs of degeneration are seen in the parasites and their numbers rapidly decrease. After two or three doses they disappear from the peripheral blood altogether.

Owing to its slow excretion atebrin, when given intravenously, appears to exert a more prolonged action than quinine on *P. knowlsi*. Our observations show that intravenous injections of quinine are not effective against a heavy infection with this plasmodium in *M. mulatta* unless they are repeated at short intervals, say of three or four hours, but one injection of atebrin suffices. It would appear that the growth of the parasites is not checked by

quinine, probably because of its rapid excretion after intravenous injection.

Dosage.—A monkey of 5 kilogrammes body weight or even smaller animals can stand a dose of 0.025 and 0.05 gramme of atebrin, intramuscularly without any untoward effects. By the intravenous route however doses larger than 0.025 gramme often produce death and we lost two monkeys in this way in the early part of our studies. As the intravenous route has no advantage with atebrin we now use intramuscular injections of 0.025 to 0.05 gramme of this drug in our experimental work. Such doses are very well tolerated and are relatively very large compared with the safe dose of 0.1 gramme thrice daily given in adult human beings of 50 to 60 kilogrammes body weight; this shows that the toxicity of the drug is low.

Relapses.—Atebrin has earned a great reputation as a powerful remedy in preventing relapses in all species of human malaria. Green (1932), treated 15 cases with 0.1 gramme of atebrin thrice daily for five days with no relapses, while there were 13 relapses among 24 controls treated with quinine. James and his colleagues (1932) treated 15 experimentally infected cases with similar doses and only one relapsed; four of them were chronic cases and had several relapses previous to treatment with atebrin. Five cases infected at Horton with the malignant 'Rome' strain of *P. falciparum* had no relapse after a course of atebrin, but two controls treated with quinine relapsed. Similar results have been recorded by Sioi, Hooper, De Uells, Jains and many others. In view of this evidence, the drug would appear to be more effective than quinine in curing malaria and preventing relapses, but so far as relapses are concerned this is not our experience with the Indian strains of malaria.

Whatever may be the case with human malaria, in monkey malaria relapses undoubtedly occur. In *M. mulatta* infected with *P. knowlsi* even after 5 days intensive treatment with large doses of the drug, the parasites invariably reappeared in 10 to 15 days and multiplied with the same rapidity as in the primary attack, causing death of the animal if prompt treatment is not given. The recrudescence can however be checked much more easily than the original attack. One dose as a rule suffices to control the multiplication of the parasites though a low grade of infection persists for a long period. A perusal of tables I to X will show that in the first relapse, if not treated, the parasites show just as great a virulence as in the primary infection, and they increase in number with great rapidity, causing death of the animal. At this stage one dose of atebrin usually suffices to stop the growth of the parasites and prevent a fatal termination. After such a dose the parasites appear to lose their virulence and either a scanty infection may persist or the parasites may disappear from the

(Continued at foot of opposite page)

STUDIES ON INGUINAL GRANULOMA*

II. THE BACTERIAL FLORA OF GRANULOMA

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A DETAILED study of the bacterial flora met with in cases of inguinal granuloma was undertaken, since the question of the ætiological agent has not yet been settled. In all, eighteen cases clinically diagnosed as granuloma were studied. In each case a dark-ground examination was first made by the venereal surgeon for *Treponema pallida*, and only cases that were proved negative are included in this study. The clinical diagnosis had to be subsequently revised in three cases, one of which proved to

(Continued from previous page)

peripheral circulation for long periods without further treatment. Whether in course of time they will regain their virulence is now being studied.

Toxic symptoms.—One of the 10 monkeys passed liquid stools for two days after 4 injections of 0.05 gramme each and showed disinclination for food. There was no inflammatory cell exudate in the stools but they contained active motile *E. histolytica*, an *Enteromonas* sp and a few *Balantidium coli*. These protozoa are often found in apparently healthy animals of this species. Diarrhœa stopped spontaneously as soon as atabrin was discontinued. Two monkeys developed slight yellow coloration of the skin of the palms of the hands and conjunctivæ but this did not persist. The yellow tinge disappeared a few days after atabrin was stopped. No symptoms showing involvement of any other organ were observed.

REFERENCES

- Chopra, R. N., Das Gupta, B. M., and Sen, B. (1933). Atabrin in the Treatment of Indian Strains of Malaria. *Indian Med. Gaz.*, Vol. LXVIII, p. 425.
Green, R. (1932). A Report on Fifty Cases of Malaria treated with Atabrin. *Lancet*, Vol. I, p. 826.
James, S. P., Nicol, W. D., and Shute, P. G. (1932). A Study of Induced Malignant Tertian Malaria. *Proc. Roy. Soc. Med.*, Vol. XXV, Part II, p. 1153.
Knowles, R., and Das Gupta, B. M. (1932). A Study of Monkey Malaria and its Experimental Transmission to Man. *Indian Med. Gaz.*, Vol. LXVII, p. 301.
Napier, L. E., and Campbell, H. G. M. (1932). Observations on a Plasmodium Infection which causes Hemoglobinuria in Certain Species of Monkeys. *Indian Med. Gaz.*, Vol. LXVII, p. 246.
Sinton, J. A., and Mulligan, H. W. (1933). A Critical Review of the Literature Relating to Identification of the Malarial Parasites Recorded from Monkeys of the Families Cercopithecidae. *Records Malaria Survey, India*, Vol. III, p. 381.

*Rearranged by Editor.

be an epithelioma on pathological examination, while another proved to be a case of ulcus molle serpinosum in which Duerrey's bacillus was found. The third case proved to be an unusually chronic type of chancre, which subsequently gave a strongly positive Wassermann reaction and promptly responded to neosalvarsan. Our bacteriological findings in the remaining fifteen cases are given below:—

Spirochætal organisms.—*T. schaudinni* in company with *Bacillus fusiformis* was found in two cases, *T. refringens* was found six times and *T. minuta* once. We did not find *T. aboriginalis* which has been found by Cleland (1909) in granuloma.

In ten cases we found Hoffman's bacillus which is recognized as a common secondary saprophyte in lesions of the genitalia, and in two instances we found an organism resembling *B. diphtheria*. Both of these bacilli were non-pathogenic to guinea-pigs.

Staphylococci were found in twelve of the fifteen cases, but streptococci were only isolated from one case.

A Gram-negative coccus occurring singly or in staphyloid groups was found in smears in four of our cases. Pure cultures were grown from two of the cases. The colonies resembled those of streptococci at first, but they gradually became larger and more opaque reaching a diameter of about one millimetre in seventy-two hours. Microscopically they resembled staphylococci in their arrangement, but individual organisms were smaller. Injected subcutaneously into a white rat they appeared to be non-pathogenic for they produced only a slight local reaction which had disappeared in forty-eight hours.

We found *Bacillus coli* on two occasions only, but this is possibly because we got rid of surface contaminating organisms by cleaning the ulcers with saline dressings for some days before examining them bacteriologically. This also possibly explains our failure to find *B. lactis aerogenes* var. *encapsulatus* which Castellani and Mendelson (1929) consider to be frequently found in inguinal granuloma.

B. pyocyaneus was found in two cases and *B. proteus vulgaris* in one case.

Plump diplo-bacilli, Gram-negative, 2.5–3µ by 1–1.5µ in size occurring almost invariably in pairs and occasionally in short chains were occasionally met with in smears. They occurred in five of our cases. Photomicrograph I shows these organisms lying side by side with a cluster of the Donovan organisms. Growth occurred on rabbit's blood, but the organism has not been isolated in pure culture. This organism is probably identical with a diplo-bacillus that is normally found in the urethra.

Leptothrix-like filaments have been occasionally met with in culture on Norris' medium, but are infrequent. Yeasts have also been met with in smears infrequently.

B. ducreyii, the causative organism of soft sore, has been put forward by MacDonagh (1920) as the probable ætiological agent. Walker has cultivated a capsulated organism from cases of granuloma and MacDonagh suggests that this might be a capsulated variety of *B. ducreyii*. Ulcus molle serpiginosum bears some resemblance to granuloma. The chief distinction is that the process is more acute than granuloma. This view is certainly of great interest since the racial distribution of the disease, its strict limitation to particular classes and its great prevalence among abori-



Photomicrograph I.—Large plump diplo-bacilli near a cluster of extracellular Donovan bacilli (X2000).

ginal races, all suggest the possibility of a variation in type from soft sore. De Monbreun and Goodpasture (1931) have found Ducrey's bacillus in three out of six cases studied. In order to test the correctness of this view, a careful examination was made of smears from the edge of the ulcers for the chain forms of Ducrey's bacillus, which are characteristic of soft sore. These were not however found in any of our cases except the one that was proved to be soft sore subsequently. An attempt to culture the organism was therefore carried out in six of our cases, defibrinated rabbit's blood mixed with 2 per cent agar being used as the medium. The medium was prepared in the proportion of 30 per cent of rabbit's blood in agar and the tubes were inoculated on the same day. Whole blood was also used. In all cases the typical chain forms of the organism could not be demonstrated.

The Donovan organism was demonstrated in smears in fourteen of the fifteen cases studied. In one case where the smear was negative, extensive healing had occurred and there was little ulceration. The organism however was recovered in culture. Out of the thirteen cases in which cultures were carried out, the organisms

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STUDIES ON INGUINAL GRANULOMA

III. THE DONOVAN ORGANISM OF GRANULOMA

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THE presence of small intracellular bodies were first noted by Donovan (1905) in a case of granuloma occurring in the mouth. He had frequently noted the occurrence of this organism in cases of granuloma inguinale. As they appeared to undergo intracellular multiplication he looked upon them as protozoa, but confessed he was unable to put them into any definite group. Subsequent workers particularly Walker (1918) and, more recently, Goldzieher and Peck (1926) have pointed out that the Donovan body is not protozoal. Walker succeeded in cultivating an organism, a capsulated diplococcus which he believed to be identical with the Donovan body. It was often bacillary in shape, sometimes coccoid and when appearing inside cells seemed to possess a capsule. He therefore concluded that the organism belonged to the mucosus-capsulatus group. Subsequent workers following modern nomenclature called it *Klebsiella granulomatis*. The organism was held to be allied to the capsulated bacillus of rhinoscleroma and the similarity of the lesion to rhinoscleroma was put forward. Other workers particularly MacIntosh (1926) have confirmed the frequent presence of the Donovan body in granuloma. He experimentally inoculated a volunteer with ground-up material and produced an ulcer which healed subsequently. Campbell however was unable to confirm these results. He cultured the organism on Sabouraud's medium and inoculation experiments were entirely negative. De Monbreun and Goodpasture (1931) in subsequent experiments claim to have transmitted the disease to a monkey by inoculation of tissue containing the organism. A small nodule developed at the site of inoculation and the organisms were demonstrated inside the cells. The question of the experimental transmission of a disease by transplantation of pathological tissues is always

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were found in culture in twelve and were isolated in pure culture in ten cases. Contamination with other organisms gave rise to difficulties in isolation in the other three cases.

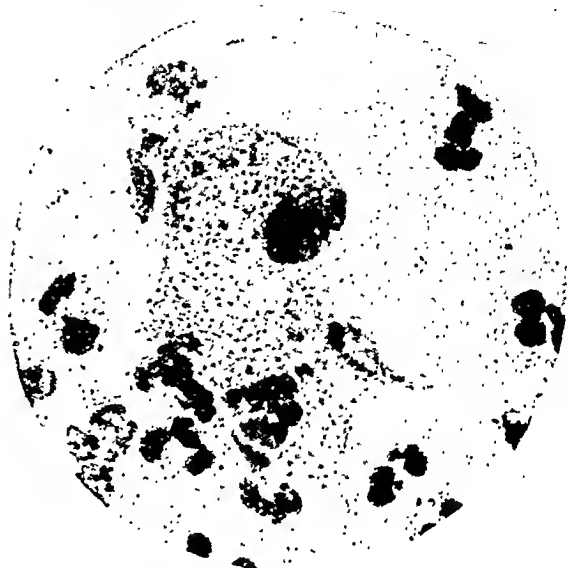
REFERENCES

- Castellani, A., and Mendelson, R. W. (1929). *Journ. Trop. Med. and Hyg.*, Vol. XXXII, p. 148.
Cleland, J. B. (1909). *Ibid.*, Vol. XII, p. 143.
De Monbreun, W. A., and Goodpasture, E. W. (1931). *South. Med. Journ.*, Vol. XXIV, p. 588.
MacDonagh, E. R. (1920). *Venereal Diseases: Their Clinical Aspect and Treatment*. London: W. Heinemann, Ltd.

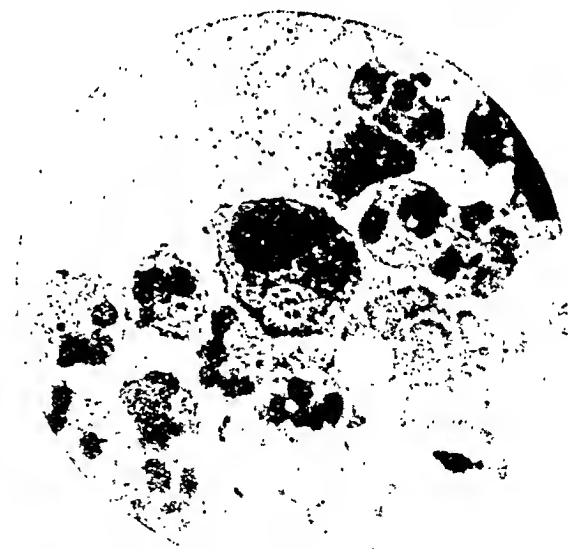
open to the objection, as Campbell rightly pointed out, that other organisms present might be included. Inoculated tissues might be slowly absorbed and generally provoke a foreign body reaction, and any included organism, particularly intracellular forms, might be recovered at a later period; such a phenomenon is well known in the case of *M. lepræ*.

In the present study it was found that the organisms could be easily demonstrated in smears taken from the surface of ulcerative lesions. In cases where healing had occurred as a result of treatment, they were difficult to demonstrate. Material for examination was taken only after the ulcer had been cleaned by a few days' saline dressing. A loopful of the serous discharge was spread evenly on a slide by means of a platinum loop so that the large mononuclear cells and leucocytes were left intact. The film was then fixed by heat and stained by Gram's method or one of its modifications. The organisms appear as small Gram-negative plump cocco-bacilli about 1.5μ in length by 0.6 to 0.8μ in thickness. They are not well stained by methylene blue or Leishman's stain. Sometimes forms almost coccoid in shape are met with. The most common forms are bacillary in shape with a tendency to bipolar staining. Dumb-bell forms also occur, but all these are of the same size. The organisms are found in clumps, most often extracellular and surrounded by a clear space of some unstained material. Intracellular forms are found in the mononuclear cells or in polymorphonuclear leucocytes. Inside the cells the outlines of the organisms are not clear and they appear to be surrounded by an unstained empty space which looks like a vacuole or a 'foamy' area in the protoplasm. No true capsule is formed and none can be demonstrated by capsule staining, but they appear as if surrounded by some mucinoid material. The occurrence of intracellular clusters which are feebly stained, with disintegration of the cell suggests intracellular multiplication. Extracellular forms, however, are more common. In some smears, where the serum has been fixed by heat, all the organisms and cells may appear as if surrounded by capsules, but this is evidently the result of fixation. The shape and general appearance, and the presence of bipolar staining suggests a resemblance to Ducrey's bacillus, but chain forms are never met with. The foamy degeneration of the cell is shown in photomicrograph I, while vacuolation is shown in photomicrograph II. It is difficult to decide whether these appearances are due to phagocytosis. The organism is non-acid-fast, is Gram-negative and is easily stained by weak carbol fuchsin. In our study of fifteen cases the intracellular forms of the organism were found in ten cases while four of the remaining five showed extracellular forms. In one case, healing had occurred and no organisms could be demonstrated in smears. Aspiration of the unruptured lesion in the last case showed

the organism in small numbers. In histological sections the organisms are difficult to demonstrate if stained with hæmatoxylin, but if the tissue is fixed in alcohol and stained by Weigert's modification of Gram's stain, they can be demonstrated in the swollen endothelial cells of the capillaries.



Photomicrograph I.—Donovan bacilli inside a mononuclear cell which has burst. Note the degeneration of the protoplasm and the appearance of the organisms—coccoid, dumb-bell and bacillary forms ($\times 2,000$).



Photomicrograph II.—Donovan bacilli inside a cyst in a mononuclear cell ($\times 2,000$).

Cultivation.—For purposes of cultivation small pieces of tissue were scraped out and inoculated into various media, after the ulcer was clean. The media that were used, were plain agar, broth, serum agar, maltose agar, lactose agar, glucose agar, Crowe's medium, blood-streaked agar, Norris' medium and defibrinated rabbit's blood mixed with agar, as for Ducrey's bacillus. Primary cultures commonly

show *Staphylococcus albus* or diphtheroids which overgrow the other organisms. It was found that Norris' medium was of great use for primary culture, since all the colonies were extremely small, and there was no danger of overgrowth. Growth occurred quite well on blood agar and on chocolate agar though not quite so profusely as on maltose agar. The hæmophilic tendency that is shown by Ducrey's bacillus is not present, since the organism grew well on media which did not contain blood. Subcultures on broth were used before further differentiation. Growth was profuse on lactose agar, but no growth occurred on glucose agar or on serum agar.

Out of the fifteen cases studied cultures could not be carried out in two cases, as they left the hospital. In one case extensive healing had occurred and the organism could not be demonstrated in smears, but was isolated in cultures. In one case contamination with a coliform organism gave rise to difficulty in culture. In two cases the organisms were recognized in cultures but could not be isolated owing to contamination with *B. proteus* in one and *B. pyocyaneus* in the other.

Cultural characters.—On Norris' medium the colonies in 24 hours were glistening, convex, transparent, and extremely small, being invisible to the naked eye but appearing under the lens as pin-points. They were just visible in 72 hours. Under the lens there was a slightly wavy border and a central translucent boss. The surface was smooth and shiny, but gradually grew dry and slightly granular. On media containing blood however the colonies were much larger, varying in size from 0.3-0.4 mm. in 24 hours and appearing as low convex, rounded, shiny areas which gradually grew somewhat opaque. There was slight hæmolysis. On plain agar and maltose agar in subcultures the colonies were still larger (the size of a pin-head) in 24 hours, having a mucoid translucent appearance and showing a tendency to confluence. The growth was profuse and gradually grew more opaque and somewhat yellowish-brown in colour. On maltose in old cultures a tendency to form a crenated border was noticeable. On broth there was a slight uniform turbidity in 24 hours and a slight deposit appeared in three days. Pellicle formation was absent, and there was little surface growth. There was a characteristic odour. In all cases the colonies were soft and in young cultures easily emulsifiable, but they gradually grew slightly dry and sticky. The organisms retained their viability on Norris' medium for about fifteen days. They died out much more rapidly on maltose agar and plain agar. Growth was best at blood heat, and under aerobic conditions.

Morphology.—Young strains isolated were non-motile, but at lower temperatures sluggish motility was observed, especially in subcultures. The organism is a non-acid-fast, Gram-negative,

small, somewhat plump cocco-bacillus, slightly oval or fusiform in shape with slightly bulging sides. Most strains show a tendency to bipolar staining. There is no evidence of the presence of a capsule on staining either by Malone's or Hiss's method, though the staining is rather indistinct with young cultures, particularly with methylene blue. Dumb-bell forms appear to be merely an exaggeration of the bipolar staining and might be preliminary to division. The organism is very small, about 1.5μ in length by 0.6μ to 0.7μ in thickness. Coccoid forms met with in smears are not common in culture unless degeneration has occurred. Metachromatic granules are absent. Spore formation is absent. In general there is a great resemblance to the morphology of *B. ducrey*. The cultural characteristics of the two organisms however show marked differences, especially in the hæmophilic tendency and mode of growth. Chain forms, which are characteristic of Ducrey's bacillus, are not usual in this organism.

Biochemical reactions.—No fermentation occurred in lactose, dulcitol and mannitol; the other fermentation reactions are shown in the table below:—

TABLE

Serial No.	Glucose	Saccharose	Maltose	Salicin	Litmus milk
1	A	A	A	A	..
2	A	A	A	A	A, no clot
3	A	?	A	A	..
4	A	?	A	A	Faint A
5	A	A	A	A	Faint A
6	A	A	A	?	..
7	AG	A	A
8	AG	A	AG	A	A, slight clot

Two strains were studied regarding their power to ferment other carbohydrates. The organism was found to ferment fructose, lævulose, galactose, raffinose, dextrin, arabin, and xylose. Inulin, inositol and adonitol were unaffected. The Voges-Proskauer reaction was negative and indol formation was absent.

Pathogenicity.—Subcutaneous inoculation into white rats was followed by rapid necrosis with the formation of a chronic ulcer, which gradually healed. In guinea-pigs a more chronic reaction occurred. These will be discussed in the next part of our studies.

Nomenclature.—The name *Calymmatobacterium granulomatis* suggested by Aragao and Vianna (Karsner, 1926), and the allocation to the group *Klebsiella* are both incompatible with the structure and relationships of this organism. In view of the morphological resemblance to Ducrey's bacillus and the uncertainty of the grouping of Ducrey's bacillus it is suggested that the name *Bacillus donovani* be applied.

Summary.—The presence of the Donovan body in fourteen out of fifteen cases studied confirms the findings of numerous observers of

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BACILLÆMIA IN LEPROSY

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THIS subject is one to which considerable attention was paid in the past. We have traced about eighty references to this subject in the literature of leprosy, most of the articles being written between 1890 and 1916. This interest in the subject was stimulated by the fact that many leprosy workers considered it possible that leprosy was transmitted by biting and blood-sucking insects; if lepra bacilli could be found in the circulating blood the theory of insect transmission would receive some support. During recent years this transmission theory has fallen into the background (though it has not been finally disproved) and, consequently, interest in bacillæmia has somewhat declined.

The matter was also studied in connection with the possibility of congenital infection of the fœtus *in utero* by the blood of leprosy mothers, and lepra bacilli have been reported in the placenta, in the blood of the umbilical cord and in the internal organs of still-born

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the close association between this organism and the disease. In ten out of twelve cases an organism resembling the Donovan body has been isolated in pure culture. It is suggested that this organism, which is a small bacillus showing bipolar staining, is identical with the Donovan body and the name *Bacillus donovani* is also suggested. The morphological resemblance of this organism to *B. ducrey* is brought forward. Animal inoculations show that this organism is distinctly pathogenic.

The writers are greatly indebted to the officers in charge of the venereal clinics at the General and Royapuram Hospital, Madras, for their kind co-operation in making this investigation possible. The bacteriological media were all supplied through the kindness of Lieut.-Colonel H. H. King, I.M.S., Director, King Institute, Guindy, to whom the writers tender grateful thanks.

The photomicrographs were all taken by Mr. Solomon, photographer, King Institute, Guindy, to whom thanks are due.

REFERENCES

- De Monbreun, W. A., and Goodpasture, E. W. (1931). *Amer. Journ. Trop. Med.*, Vol. XI, p. 311.
 Donovan, C. (1905). *Indian Med. Gaz.*, Vol. XL, p. 411.
 Goldzieher, M., and Peck, S. M. (1926). *Arch. Path.*, Vol. I, p. 511.
 Karsner (1926). *Human Pathology*. New York: J. B. Lippincott Company.
 MacIntosh, J. A. (1926). *Journ. Amer. Med. Assoc.*, Vol. LXXXVII, p. 996.
 Walker, E. L. (1918). *Journ. Med. Res.*, Vol. XXXVII, p. 427.

children [Chujo (1916), Sugai and Mononobe (1913), Rodriguez (1926), Pineda (1927)].

There is no doubt that bacilli enter the blood stream. The occurrence of multiple lesions in various parts of the body can only be explained by the bacilli being conveyed in the blood. This does not mean that the blood of leprosy cases normally shows bacilli, for bacilli may only enter the blood stream very occasionally and only in very small numbers. The possible means by which bacilli enter the blood are (a) by the lymph vessels opening by the lymphatic duct into the left innominate vein, (b) by the erosion of a leproma into a blood vessel, and (c) by infected wandering histiocytes entering the blood stream. Which of these three means is the most important it is difficult to say, for there is little evidence on this point. Lepromata normally show little tendency to erode into blood vessels, so the two other modes of entry seem more likely.

Recently, interest in bacillæmia has been somewhat revived by the writings of certain workers who claim to find bacilli in the blood of early cases of leprosy and even of 'contacts', and who have recommended blood examination for bacilli as an important aid in diagnosis and even as the best method of diagnosis.

Brief survey of the literature

It is impossible here to survey thoroughly the mass of literature on the subject of bacillæmia. We will here refer to only the more important publications.

The technique used by different workers varies. Some workers have used the thick-film method, puncturing an apparently unaffected area of skin, making a thick smear on a slide, drying, de-hæmoglobinizing with dilute alcohol or distilled water, and staining by the Ziehl-Neelsen method. Other workers have taken the blood from a vein, separated the red cells either by sedimentation or by hæmolyzing agents, and examined the white cell deposit. Two methods have been commonly used, those of Crow (1912) and Rivas (1912).

The technique of Rivas is as follows:—

Collect 0.1 c.cm. to 1 c.cm. of blood from a vein in 5 c.cm. to 20 c.cm. of 2 per cent acetic acid solution, in which the erythrocytes are dissolved. The mixture is centrifugalized for 15 minutes. The sediment is spread on a slide, dried, stained and examined.

Crow's technique:—Take 5 to 10 c.cm. of blood from a vein into a sterile test tube containing 5 to 10 c.cm. of 2 per cent sodium citrate in normal saline. Mix thoroughly, and leave overnight in an ice box. The next day there will be found three layers, at the bottom a thick layer of red cells, in the middle a thin layer of leucocytes, and above the serum and citrated saline. Make thick smears by removing some of the leucocyte layer in a capillary pipette. Dry, de-hæmoglobinize any red cells.

present by treating with distilled water for 15 minutes. Dry again, stain and examine.

Results reported

In 1896 Stephan reported a case of maculo-anæsthetic leprosy in which *M. lepræ* were found in all of sixty thick smears, thirty from macular lesions and thirty from apparently healthy skin, and he considered that this proved that the bacilli were free in the blood stream. Various later workers criticized this conclusion, for they said it merely showed that bacilli were present in the skin and not necessarily in the general circulation. Most of the workers after this took the blood from a vein.

Doutrelepoint and Wolters (1896) found bacilli in the blood of all cases of lepra reaction and not in others. Several other workers have verified this. Babes (1901) failed to find bacilli in the blood in lepra reaction but did find them in one non-febrile case.

Crow (1912) reported 21 positive findings in 24 cases. Later he reported 8 positive findings in 10 cases after taking all precautions to prevent false positives. Takasawa (1911) reported 12 positive out of 31 cases. Marchoux and Bourret (1909) failed to find any bacilli in the blood stream. M. Chujo (1911) reported 14 positive findings in 27 cases, the largest number of bacilli being 12 and the average 3. Half the organisms were found free and half inside leucocytes and large mononuclears. Ohashi (1911) reported 80 per cent positive findings in lepra tuberosa and 22 per cent in lepra nervosa. Honeij (1915) reported, in 28 examinations of 16 patients, 9 positive results, 3 questionable, and 16 negative. Mitsuda (1911) in 31 cases of lepra tuberosa found 12 positive. Two cases of lepra reaction showed large numbers of bacilli. Iyengar (1919) reported finding lepra bacilli in the blood of 4 out of 10 cases of nodular type, 1 out of 20 of anæsthetic type, and 2 out of 10 of mixed type. Two nodular cases showed bacilli in the blood from the skin, but not in the nodules. Rivas and Smith (1914) using the thick film method in three cases found many bacilli in the blood from the lesions and a few in the blood from the fingers and toes which were unaffected. Blood from veins also showed a few bacilli. They considered this as a very definite proof of bacillæmia. Such reports can be multiplied indefinitely.

The first really critical examination of the subject is that of Hollmann (1916). After a brief survey of the literature he reported on the examination of 22 cases by the technique of Crow and of Rivas. The blood was taken from an arm vein and the puncture made through apparently healthy skin. Not trusting to appearances, after taking the blood from the vein he made scrapings and smears from the puncture hole in the skin. He reported as follows:—Of 17 nodular cases six showed bacilli in the slide made from the blood. Of 5 anæsthetic cases none showed bacilli. The largest

number of bacilli seen was 7 and the smallest 1. Of the six cases (all nodular) giving positive results in the blood, 5 showed bacilli in the apparently normal skin at the site of puncture. Hollmann said 'It is possible that the needle puncture may have become infected with acid-fast bacilli from the blood when the needle was withdrawn'. He does not seem to have seriously considered the other explanation, namely that the blood was infected by the needle which had passed through infected skin. The explanation seems to us to be a far more likely one. Although the evidence seems fairly clear, the logical conclusion, that many positive results reported are false positives due to infection of the blood from infected skin at the site of puncture, does not seem to have been drawn.

Markianos (1931) using the thick film method found that bacilli were found only when the puncture was made through affected skin. Unaffected skin showed no bacilli in the thick blood drop. He considered that positive findings in the film were due to the blood washing out bacilli from the lymph spaces in the infected skin at the site of puncture. Nevertheless he considered that the thick film method of bacteriological examination of leprosy lesions was a useful procedure in diagnosis. Mitra (1932) using the thick film method reported positive findings in unaffected skin in 21 out of 26 cases. He described the thick film method as a new method of diagnosis of leprosy. Sardjito and Sitanala (1932) using the thick film method in unaffected skin found bacilli in 35 out of 38 cutaneous cases, and in 3 out of 14 nerve cases. Of 129 healthy contacts 6 gave positive results, in one case as many as 50 bacilli in one microscope field. They found that the thick film method taking the blood from a finger showing no leprosy lesions gave a higher percentage of positive findings than either nasal examination or examination of the skin of the ear lobe.

Discussion of these findings

It will be seen that these findings vary so tremendously that it is very difficult to assess their value. There are so many difficulties and fallacies. The principal factors causing these differences in findings are:—

1. *Variation in the type and stage of the disease.*—Bacillæmia is commonly reported in cutaneous leprosy and rarely in nerve leprosy. It is reported to be much more common in cases of reaction than in other cases.

2. *Differences in technique.*—Some methods involve the examination of the deposit from 0.1 c.cm. of blood. Other methods of 10 c.cm. of blood. Results naturally vary.

3. *The difficulty of avoiding contamination of the blood from infected skin at the site of puncture.*—This difficulty is very great and we believe that it probably accounts for many of the positive results reported. In cases of leprosy, areas of skin which appear normal often show definite lesions and numerous bacilli

on pathological examination. Several such cases have been reported by Lowe and Christian (1932) and one such case by Muir (1932). In a case of leprosy, it is impossible to tell from mere inspection whether skin is affected or not. The only sure method of excluding skin infection is to cut out the piece of skin for section and this is not a practical procedure in many cases. One has to rest content to make slit scrapings and smears of the skin at the site for puncture. When this is done, as reported by Hollmann (1916), it is found that nearly all the cases showing bacilli in the blood show bacilli in the skin at the site of puncture, and thus grave doubt is thrown on the accuracy of the findings of bacilli in the blood.

Recent publications claiming to have demonstrated bacillæmia by thick film methods ignore the possibility of the bacilli coming from the skin and the only precaution taken to prevent this is naked-eye inspection. 'The skin appears normal' is the usual report but this is absolutely unreliable. We have seen dozens of 'normal' areas of skin in which millions of acid-fast bacilli could be found. In fact in many cases of cutaneous leprosy it is difficult or impossible to find unaffected skin in a site suitable for puncture.

The failure to realize these facts makes most of the past work on bacillæmia of very doubtful value. Since blood examination has been recommended as an important aid in diagnosis, the matter is not purely an academic one. It therefore seems desirable that a fresh investigation of the subject should be made, taking all precautions against false positive findings, examining cases at all stages of the disease, and using as standard the method which is found to give the greatest number of positive findings.

Investigation of the thick blood film method of finding Hansen's bacillus

Experiment 1.—One hundred cases of neural leprosy were examined by the thick film method, a finger being pricked by a needle to make the film. In not a single film were any acid-fast bacilli found.

Experiment 2.—Fifty cases of cutaneous leprosy were similarly examined. Seventeen showed bacilli in the thick film. These were all advanced cutaneous cases. Of these seventeen, ten showed visible skin lesions in the skin of the finger, and in the other seven, smears taken from the skin at the site of the prick showed in every case many more acid-fast bacilli than were found in the thick film.

These two experiments show quite clearly that the thick film gives positive results when the skin at the site of the prick is leprosy, and that naked-eye inspection of the skin is not a reliable method of detecting slight leprosy skin lesions. The slit smear method used in the same site shows far more bacilli than the thick blood film method and this suggests that the bacilli in the thick blood film come from the

skin at the site of the prick, and not from the circulating blood.

A further small test of this method was made.

Experiment 3.—Ten cutaneous cases were chosen all being of the milder type (C_1 or C_2) and all showing no outward sign whatever of leprosy lesions of the finger. Thick films were made from the finger and also at the same time slit smears from the skin about one quarter of an inch away from the site of the prick.

Of 10 cases, 7 showed bacilli in the thick blood film.

Of 10 cases, 8 showed bacilli in the slit smear.

None showed bacilli in the thick film without showing them also and in far greater number in the slit smear.

This experiment showed fairly clearly that the bacilli came from the skin and not from the circulating blood; but to test the matter still further another experiment was done.

Experiment 4.—In the above seven cases showing bacilli in the thick blood film, the venous blood was taken and examined for bacilli by the technique to be described later. In only one case were bacilli found. We think that this shows fairly conclusively that in most cases bacilli found in thick blood film come from the skin.

Examination of the venous blood for bacilli

Technique.—It is not easy to develop a suitable technique. An examination of the literature on tuberculosis reveals the fact that dozens of different methods have been recommended by different workers. This is a clear indication that there is no one simple reliable method. A suitable method should use a fairly large quantity of blood and reduce it to a small amount of residue. The chief difficulty which is encountered is the precipitation of albumen which occurs when acid or alkali is added to destroy the cells.

The following method, which we have adopted after testing many different methods, has given us the most satisfactory results. With a sterile syringe and needle the antecubital vein is punctured in an area of apparently healthy skin and 4.8 c.cm. of blood are drawn off and evacuated at once into a sterile centrifuge tube containing 1.2 c.cm. of 5 per cent sodium citrate. The tube is shaken to mix the two fluids, and then centrifuged thoroughly. The supernatant fluid is then carefully removed with a sterile capillary pipette, and the blood cells are left. To this residue about 7 c.cm. of 25 per cent alcohol is added and the tube thoroughly shaken. This de-haemoglobinizes the red cells. The tube is then centrifuged for ten minutes, and the fluid is again pipetted off. Only the white cells are now left. To this residue add 1 c.cm. of 10 per cent antiformin and shake thoroughly. This dissolves the white cells and at the same time precipitates some albumen. Leave the tube standing for 5 to 10

minutes until the cells are completely disintegrated. Then add about 6 c.cm. of 30 per cent alcohol, mix thoroughly and centrifuge again. Pipette off the fluid. A small amount of white residue is left at the bottom of the tube. This consists of cellular debris and bacilli if present. Smears of this residue are made with a platinum loop and a little egg albumen on a microscope slide, fixed by heat, stained and examined. Two hundred fields were carefully examined in every case.

Experiment 5.—Twenty-three cases of neural leprosy were examined by this technique. In two cases acid-fast bacilli were found, in one case only 2, and in the other case 3.

Experiment 6.—Fifty-one cases of cutaneous leprosy were examined by this technique. In 28 cases bacilli were found. These were nearly all marked cutaneous cases and the number of bacilli was very small.

This experiment shows that this method of examination of venous blood gives a far higher percentage of positive findings than does the thick film method. This is only what one might expect since a far greater volume of blood is examined. The question still remains however as to the possibility of these bacilli getting into the blood from the skin at the site of vein-puncture. This matter was investigated.

Experiment 7.—In 21 cases all showing bacilli in the blood taken from a vein by the above technique, slit smears were made of the skin at the site of vein-puncture. It should be noted that in all these cases the skin at the site of vein-puncture appeared perfectly normal on inspection and palpation. Of the 21 cases, 15 showed bacilli in the skin; in several cases they were quite numerous and in every case more numerous than in the film made from the venous blood. It therefore appears quite probable that some of the positive findings in experiment 6 are false positives caused by a few bacilli in the skin contaminating the needle and the blood from the vein.

Conclusions

From these experiments we draw the following conclusions:—

1. The finding of bacilli in the circulating blood of cases of neural leprosy is very rare.

2. The finding of bacilli in the circulating blood of cases of cutaneous leprosy is commoner.

3. The thick film method of detecting bacillæmia in the blood is extremely unreliable, nearly all the positive results reported being false positives due to the prick being made in leprotic skin.

4. Examination of the venous blood by a concentration method as described is much more reliable, showing bacilli very occasionally in neural cases, and commonly in cutaneous cases, particularly in marked cutaneous cases,

but it is probable that some of these findings are false positives.

5. Examination of venous blood for lepra bacilli is a complicated and difficult procedure and quite unnecessary for diagnosis.

6. Other methods of bacteriological examination particularly skin examination by the 'slit' and 'clip' methods are far easier and far more reliable than blood examination.

One very interesting point to which we have previously referred but which the present investigations have demonstrated very clearly is the very frequent finding in definite cases of leprosy of acid-fast bacilli in apparently unaffected areas of skin. In cases of cutaneous leprosy the involvement of the skin is very much more extensive than the clinical lesions would indicate. In practice we find that in marked cases of cutaneous leprosy, although the visible lesions are confined to certain areas of the skin, yet practically all the skin of the body may be involved; hence it is difficult or impossible to puncture a vein through unaffected skin.

REFERENCES

- * Babes, V. (1901). *Die Lepra*, Vienna.
- * Chujo, M. (1916). *Japan Journ. Dermat. and Urol.*, Vol. XVI, p. 16.
- * Crow, G. B. (1912). *United States Naval Med. Bull.*, Vol. VI, p. 25.
- * Doutrelepon and Wolters (1896). *Arch. Dermat. u. Syph.*, Vol. XXXIV, p. 55.
- Hollmann, H. T. (1916). *Pub. Health Bull.*, No. 75, p. 15.
- Honeij, J. A. (1915). *Journ. Infect. Dis.*, Vol. XVII, p. 376.
- Iyengar, K. R. K. (1919). *Indian Journ. Med. Res.*, Vol. VII, p. 235.
- Lowe, J., and Christian, E. B. (1932). *Ibid.*, Vol. XIX, p. 867.
- Marchoux, E., and Bourret, G. (1909). *Lepra*, Vol. IX, p. 63.
- Markianos, J. (1931). *Bull. Soc. Path. Exot.*, Vol. XXIV, p. 172.
- Mitra, P. N. (1932). *Indian Journ. Med. Res.*, Vol. XIII, p. 1.
- * Mitsuda, K. (1911). *Japan Journ. Dermat. and Urol.*, Vol. XI, p. 47.
- Muir, E., and Chatterji, S. N. (1932). *Indian Journ. Med. Res.*, Vol. XIX, p. 1163.
- Ohashi, K. (1911). *Mitt. d. Med. Gesellsch. zu Osaka*, Vol. X (abstracted in *Centralbl. Bakt. Ref.*, 1911, Vol. L, p. 143).
- Ohashi, K. (1911). *Mitt. d. Med. Gesellsch. zu Tokyo*, Vol. XXV (abstracted in *Centralbl. Bakt. Ref.*, 1912, Vol. LII, p. 482).
- Pineda, E. V. (1927). *Trans. 7th Congress, Far Eastern Assoc. Trop. Med.*, Vol. II, p. 390.
- Rivas, D. (1912). *Journ. Amer. Med. Assoc.*, Vol. LIX, p. 298.
- Rivas, D., and Smith, A. J. (1914). *Amer. Journ. Trop. Dis. and Prev. Med.*, Vol. II, p. 327.
- Rodriguez, J. N. (1926). *Philippine Journ. Sci.*, Vol. XXXI, p. 115.
- Sardjito, M., and Sitanala, J. B. (1932). *Mededeel. dienst volksgezondh. Nederl.-India*, 21st year, p. 32.
- * Stephan, K. (1896). *Inaugural Dissertation*, Kaiser Wilhelm Universität. Strassburg.
- Sugai, T., and Mononobe, I. (1913). *Trop. Dis. Bull.*, Vol. II, p. 287.
- * Takasava (1911). *Mh. Dermat.*, Vol. LII, p. 521.

* Original papers not available.

THE MECHANISM OF IMMUNITY IN MALARIA

PROOF OF THE PHAGOCYTOSIS OF MALARIAL PARASITES BY LARGE MONONUCLEAR CELLS IN MALARIA

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IMMUNITY in protozoal diseases such as kala-azar and malaria differs markedly from immunity in bacterial diseases, such as typhoid infection, in that the evidence of comparable toxin production and the demonstration of antibodies in the plasma by serological tests is not yet accepted.

On the other hand, the reticulo-endothelial system immediately falls under suspicion as the main means of destroying the parasites of kala-azar and of malaria, through the mechanism of phagocytosis, by reason of the great enlargement of the spleen and to a lesser degree of the liver in these two diseases, and by reason of the associated rise in the large mononuclear count in the blood.

In kala-azar, little or no acquired immunity develops and the natural course of an untreated case is rapidly towards death; but all laboratory workers are aware of the phagocytosis of kala-azar parasites by the reticulo-endothelial monocytes of the spleen, and of the occasional appearance of such parasite-laden mononuclears in the blood.

In malaria, some degree of immunity or tolerance is acquired after years of exposure to endemic infection; this is indicated by the diminution of the spleen, parasite and fever rate as the age of those exposed to infection throughout life increases. In malaria, as in Kala-azar, it has long seemed probable that a hypertrophy of the reticulo-endothelial system results in the active phagocytosis of malarial parasites and in their rapid destruction. This destruction is even more complete than with kala-azar, whence the relative innocence of malarial infection. Fortunately, the malarial parasite produces an easily recognized pigment and thus furnishes abundant proof of the phagocytic activity of the reticulo-endothelial cells in severe malaria in that smears from the spleen, liver and bone-marrow show phagocytosis of black or of yellow-brown malarial pigment (as was obvious in my case recorded below) whilst smears from other body organs (e.g., salivary glands, pancreas, kidney, thyroid, heart, etc.), show no such massive collections of pigment within their fixed tissue cells. The reticulo-endothelial tissues in a fatal case of acute malaria indeed provides a natural analogue of the 'blockage' of the reticulo-endothelial system with injected pigments and dyes.

Further, pigmented large mononuclear cells are not infrequently found free in the peripheral circulation in severe and chronic malaria.

But whilst the proof of pigment phagocytosis both in the fixed cells of the reticulo-endothelial system and in the peripheral circulation is obvious, the proof of the existence of malarial parasite phagocytosis in man has hardly yet been made clear. In both bird and monkey malaria experimental proof already exists of the active phagocytosis of malarial parasites in liver and in spleen smears and also, in heavy infections, in the peripheral blood.

But, until December 1932, very few cases have been recorded in which malarial parasites undergoing phagocytosis have been observed in the blood in human malaria. Indeed Chopra and Sen in reporting 'A fatal case of severe malignant tertian malaria' in the *Indian Medical Gazette* of December 1932, in which they observed 'a heavy phagocytosis of the parasites' by the large hyaline and polymorphonuclear leucocytes in the blood of a human subject half an hour before death, note that this phenomenon 'has not apparently been seen by any other workers, except by Knowles and Das Gupta (1931) who only once encountered scanty phagocytosis in a malignant tertian infection'.

But since the proof of the recognition of malarial parasite phagocytosis in man is so important a step forward in the understanding of the mechanism of immunity in malaria, I am tempted to place the following two examples which I have observed, one in 1919 and one in 1932, on record. The first case showed a small malignant tertian ring in the cytoplasm of a large mononuclear cell which I found in the blood smear of a soldier with severe malignant malaria in the brigade laboratory, Bannu, North-West Frontier of India, in 1919, and a copy of the diagram I then made is reproduced as figure 1. My 1932 case is described below:—

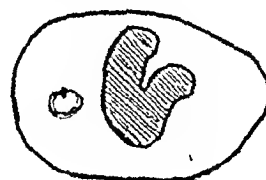


Fig. 1.

CLINICAL FEATURES

In December 1932 a well-built deeply-jaundiced male, Pahari Hindu of some 25 to 30 years, was found unconscious in a railway carriage in which there was also a dead body. The Police brought him to King George's Hospital, where he was admitted with deep jaundice in a cold and collapsed condition with a temperature of 96.4°F., a pulse rate of 98, and respirations at 22. The liver was enlarged three fingers below the costal margin and was soft and tender. The spleen was also soft and markedly enlarged. The blood was taken at 2 P.M., ten grains of quinine were given intravenously at 3 P.M. and he died at 4 P.M. in complete coma.

BLOOD-FILM EXAMINATION

Variety of parasites present.—99.5 per cent of the blood parasites were in the form of small malignant tertian rings, including many 'accollé' forms, whilst 0.5 per cent malignant tertian sporulating bodies were noted in 2,000 parasites counted. No gametes were observed in many thousands of fields examined. No large benign tertian types of rings were observed, and no benign pre-sporulating amoeboid forms. In some 15 malignant tertian sporulating bodies the merozoites numbered 14, 7, 6, 10, 7, 11, 16, 17, 7, 16, 14, 14, 15, 17, 12, with an average of 12 merozoites per sporulating body. The small rings varied slightly in size. There were many examples of multiple infections in a single red cell. The following table shows the percentage of infected red cells showing multiple infection:

M. T. Rings in the R. B. C.	INFECTED R. B. C'S. COUNTED	
	Actuals	Per cent.
1	1,384	82.5
2	236	14.0
3	35	2.2
4	12	0.7
5	1	0.1
Sporulating bodies	9	0.5
	<hr/> 1,677	<hr/> 100.0

Many rings had two chromatin dots, in one red cell three rings were seen each of which had two chromatin dots. In another red cell no less than six rings were seen, most of which had two chromatin dots. These points are brought out in the diagrammatic composite field shown as figure 2. The blood smear diagnosis therefore was an intensely heavy infection with asexual malignant tertian parasites. The clinical diagnosis was an algid type of acute malignant malaria with jaundice.

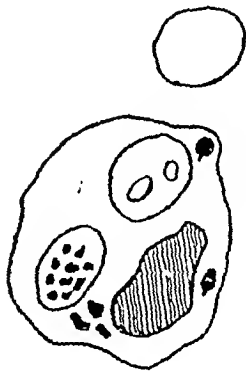


Fig. 3.

Number of parasites present.—Under the microscope every field showed a very heavy infection with parasites. At first glance it appeared as though some 50 per cent of red cells were infected, but on counting 5,000 successive red cells 34 per cent were found infected and 66 per cent uninfected.

The red cells.—These were normal in size and shape. There was no marked evidence of any rapid red-cell production or degeneration, but a few nucleated and some polychromatophilic red cells were seen. The total red cells appeared greatly decreased in proportion to the white cells present there being 65 white cells amongst the 5,000 red cells examined, but this count was made along the free edge of the film.

The white cells.—The differential count of 2,000 white cells showed, polymorphonuclears—27 per cent, large mononuclears—16 per cent, lymphocytes—56 per cent, and eosinophiles—1 per cent.

The great increase in the combined large mononuclears and small lymphocytes was very obvious. Amongst the lymphocytes were encountered a number of mononuclears of a size slightly larger than a polymorphonuclear

cell but with a large round or oval nucleus and a narrow strip of clear blue protoplasm. Many Turks' irritation cells were present. The serum gave an immediate direct positive van den Bergh's reaction.

Phagocytosis of parasites

This film contained so many parasites that it was distributed to a class of some fifty students and it was also examined by several workers in the laboratory without the mononuclear phagocytosis being observed. Once however the first example had been identified and attention was thus diverted to the blood phagocytes—many further examples were recognized. The first example seen (figure 3) showed a large mononuclear phagocytosing a sporulating body, the area around which was clear, colourless and well defined, and of the same size as the surrounding red blood cells.

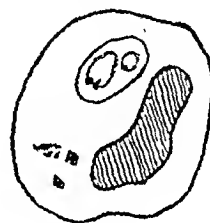


Fig. 6.

Near it and within the same mononuclear was a pink-stained red blood cell of the same tint and size as the extracellular red cells. Five masses of pigment were also seen within the cloudy cytoplasm of the cell.

A second example (figure 4) showed the process of intracellular digestion further advanced. The clear circle of the size of a red blood cell



Fig. 4

obvious in figure 3 had disappeared and a faint halo only surrounded the grouped spores the staining of which was less defined than in the previous example. An independent small ring was also seen in the cytoplasm. Another mononuclear (figure 5) showed the spores apparently scattered throughout the cell cytoplasm and their differential staining was even more obscure. In figure 6, a red cell containing two

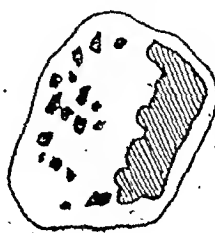


Fig. 5.

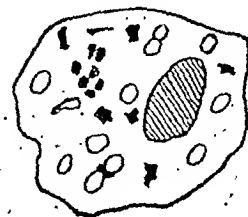


Fig. 7.

small rings had been phagocytosed. This perhaps is the usual stage previous to the finding of small rings in the cytoplasm though perhaps it is just possible that young 'accollé' parasites free in the blood may be phagocytosed and develop in the large mononuclears to ring forms. The diagrams were drawn from cells actually seen. The shape of the large mononuclear phagocytes was usually somewhat flattened oval, and the outline slightly wavy. The nucleus was usually elongated or somewhat indented. The cytoplasm was hazy and stained somewhat indefinitely whilst in it were often vacuoles, pigment and granular debris, the origin of which it was only possible to surmise. In one cell (figure 7) the semi-digested remains

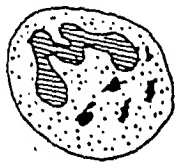


Fig. 8.

of a sporulating body could just be made out. No parasites were observed inside the polymorphonuclear cells, but in them pigment and granular debris was not uncommon (figure 8).

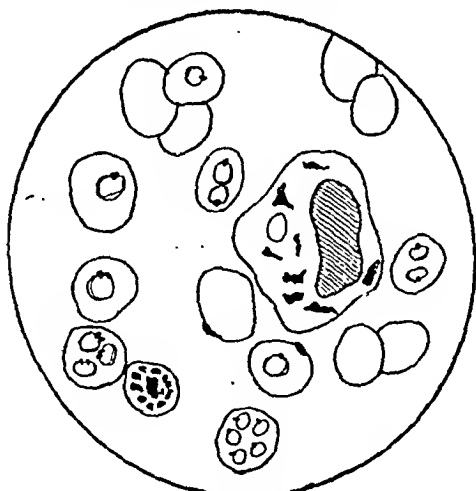


Fig. 2.

POST-MORTEM AND MICROSCOPIC SECTION REPORT

All the tissues were deeply jaundiced. The enlarged liver weighed 63 ounces, and the enlarged soft spleen weighed 15 ounces. The other organs were normal.

Microscopic sections of the spleen, liver, lung, brain, adrenals, heart, testicle, kidney, pancreas and salivary and thyroid glands were examined, but proved of interest only in that pigment was found outside the blood vessels only in those organs in which the reticulo-endothelial cells exist—e.g., pigment was scattered in large amounts throughout the spleen and also through the liver, not in the hepatic cells themselves but closely packed in the Kupffer stellate cells. The lung showed mononuclear phagocytes packed with pigment in the alveoli. The brain and adrenals showed some small amount of extra-vascular pigment, whereas the heart, testicle, pancreas and salivary glands were practically pigment free. The capillaries of all organs were full

of parasitized red cells and of pigmented mononuclears. The pigment was of two kinds (1) coal black and (2) yellowish brown which was greater in total amount. The kidney sections showed some glomerular nephritis and blood casts.

Three other cases showing parasite phagocytosis in human blood

Major Fitzgerald, I.M.S., who has had much experience of practical blood smear work in Assam, informs me that he observed two cases in which he saw malignant tertian rings within large mononuclear blood cells. Both cases showed a heavy infection of small malignant rings within the red cells and also numerous sporulating bodies in the peripheral blood which latter mainly attracted his interest. Both patients were severely ill with high fever and stertorous breathing and died in coma within a few hours of admission. The clinical diagnosis was cerebral malaria. As most patients in Assam the spleens were enlarged, but there is no recollection as to whether an enlarged liver and hæmolytic jaundice was present. I have consulted four other medical officers of special experience in malarial film work in the United Provinces but they have not observed this phenomenon. Chopra and Sen's case was clinically similar to the above; he died in coma the day after admission with fever. The total red cells were 4,680,000 of which 54 per cent were infected; the infection rate later rose to 67 per cent. Blood, two hours and again half an hour before death, showed parasite phagocytosis—chiefly schizonts by large mononuclears and polymorphonuclear cells. Thompson and Robertson in their *Protozoology* (1929) figure a polymorphonuclear leucocyte containing two mature malignant tertian segmenting forms and remark on page 52 that 'The large mononuclears, especially those of endothelial origin, are highly phagocytic and may be seen in the peripheral blood containing numerous masses of pigment. The polymorphonuclears too are also actively phagocytic and may actually engulf pigment or complete schizonts'.

Craig, C. F. (1909), in his *Malarial Fevers* says 'the endothelial cells of the liver are found in the peripheral circulation acting as phagocytes in only the most pernicious cases of malaria, but in the liver these cells are actively phagocytic'. In one or two instances I have observed entire plasmodia within coarsely granular eosinophiles.

I am much indebted to Lieut.-Col. Sinton, V.C., I.M.S., in charge of the Malarial Bureau of the Central Research Institute, who has himself observed this phenomenon of phagocytosis of malarial parasites in the peripheral circulation, for the following two references.

Firstly, Marchiafava and Bignami in their historic work entitled 'The parasites of malarial fevers', 1894—write (page 180) 'The fact that in the dangerous infections one frequently meets with blood-corpuscle-laden cells, and especially with large leucocytes containing brassy red

dissected up the peritoneum similarly to what occurs in a large broad-ligament cyst. The transverse and descending colon formed part of its wall. The peritoneum gave way above the uterus towards the right side, where the edge of a necrotic placenta appeared. The foetus was easily removed. Apart from a condition of pes calcaneus, it was well formed and weighed 5½ lbs. It was of course dead. A quantity of liquor amnii, much thickened with meconium, vernix and debris, escaped. The placenta and part of the necrotic sac was removed without difficulty. The remainder was closed over and the abdomen closed without drainage. The patient died 5 days later of peritonitis, probably on account of infection from the colon.

It is considered that in this case drainage should have been through the posterior fornix as a final step in the operation, and that the patient's life might perhaps have been thereby saved.

Tubal abortion.—Mrs. M., admitted on 30th May, 1933, for uterine hæmorrhage. She complained of bleeding from 23rd to 29th May, accompanied by pain in the lower abdomen. The pain, which was sudden in onset but not severe, was dull aching in character, varying in intensity. The bleeding was very slight for the first two days.

History.—Married 3 years; no pregnancy.

Menstrual history.— $\frac{3-4}{28}$ type, regular.

Dysmenorrhœa for the last 4 periods, with slight fever. The last period (11th to 16th May) was 10 days late. Previous periods regular.

Per vaginam: Uterus anteverted, normal in size. Right fornix hard, ovarian swelling the size of a walnut. Left fornix soft, swelling the size of a small orange. No cervicitis.

Patient admitted to hospital for observation. Slight intermittent discharge of blood continued.

Aschheim-Zondek test :—Result : weak positive on 6th June, 1933.

The patient was operated upon on 14th June, 1933, for ectopic gestation.

The pelvic peritoneal cavity contained a good deal of black blood. A tubal mole was seen protruding from the abdominal ostium of the right tube, which was somewhat enlarged and collapsed. The mole was easily expressed from the abdominal ostium by gentle pressure, leaving the tube undamaged and with only very slight oozing of blood.

The left tube was found to be closed, and its ampullary portion dilated. It appeared to be slightly inflamed. It was incised, salpingostomy being done. The patient and her husband being very anxious for a child, the right (pregnant) tube was left intact in view of the character of the left tube. A ventri-suspension completed the operation.

The patient's husband gave a suspicious history of infection and the patient was given

special treatment in view of this. She made an excellent recovery.

Ovarian pregnancy.—Mrs. C., aged 38, first seen on 26th April, 1933, for sterility; she was perfectly healthy and her pelvic organs were normal. Her last period of menstruation was on 20th to 22nd April.

A Rubin inflation of the fallopian tubes was carried out on 1st May, at a pressure of 120; both tubes were patent. Fourteen days later, when the next period was expected, the patient was seized with severe lower abdominal pain and remained two days in the nursing home. The writer happened to be out of Bombay just then and did not have the opportunity of examining her for the pain, which subsided in two days. The expected period did not arrive.

She was seen again on 31st May, with a slight uterine hæmorrhage, but no pain. She stated that, since the pain of 15th May, she could not lie comfortably on her left side.

She was not examined vaginally, as it was not thought desirable to increase the risk of a threatened abortion. She did not keep in touch with the writer, but returned on 14th June, reporting that she had miscarried on the 8th. From her description of what she passed, and the fact that she was a trained maternity nurse, I at first considered that this was probable, but on examining her I found the uterus not enlarged and a lump situated behind and to the left of it about the size of a plum, slightly tender and firm in consistency. There was pulsation between this lump and the left side of the uterus. She had a slight blood-stained discharge brownish-red in colour, and had slight pain in the lower abdomen. She was told that the condition might indicate extra-uterine gestation, was cautioned to keep very quiet, and to remain in communication with the writer. In the event of any pain or feeling of illness, she was instructed to go to the nursing home immediately.

No such developments occurred, but, under instructions, she returned on the 19th and the following condition was found :—

Slight uterine bleeding as before. Slight pain in the hypogastrium. By vaginal examination the lump to the left of the uterus was found to be enlarged to double the size noted on the 14th. She was ordered immediately into the nursing home as a case of extra-uterine gestation, and was operated on the same day.

On opening the peritoneum, there was extremely little free blood, but, on raising the sigmoid flexure, the left ovary was found enlarged to the size of a peach, deep red in colour, and with loose adhesions of blood-clot to the lateral wall of Douglas' pouch. The ovary presented exactly the appearance of a twisted ovary, or ovarian hæmatoma, clearly limited to the ovary except for the shell of blood-clot noted. There was only a little blood-stained serum in Douglas' pouch. The left fallopian

tube was absolutely normal throughout its length, its abdominal ostium being patent and entirely free from any swelling or bleeding.

On freeing the ovary, the ovarian ligament was clearly defined and tied off, and the ovary removed. Nothing else (except the appendix) was removed, as both tubes and the other ovary were quite normal. The patient made a good recovery.

The specimen was immediately examined by the operators. On incising the ovary towards its outer side, an intact gestation sac was found, deeply embedded among the blood-clot, and, on opening this, an ovum, 0.6 centimetre in length, was demonstrated. Assuming that this was an ovum of normal development, it would be scarcely a month old. Hence the questions arise: Was the patient pregnant when she missed her period on 14th May? If so, was it a second follicle which gave rise to the ovarian pregnancy and in consequence did she really have an abortion on 8th June? I am inclined to think that a menstrual corpus luteum in the left ovary was prevented from degenerating by an accidental fertilization, about the middle of May, of a second follicle in the same ovary, hence the period expected in the middle of May did not appear, and the foetus was of about five weeks' development, allowing for its being less well developed than it would be if implanted in the uterine decidua.

Repeated tubal pregnancy with twins.—It is recognized that, where pregnancy has occurred in one tube, there is a marked risk of a subsequent pregnancy occurring in the other tube, though naturally cases of this kind are scarce. The following example is of exceptional interest in view of the fact that the second tubal pregnancy presented twins.

Case.—G., was admitted under the care of another surgeon on 23rd May, 1928, with symptoms suggesting extra-uterine gestation. She was operated upon on 1st June, 1928, when a left tubal pregnancy was found and the left tube and ovary were removed.

The patient was re-admitted under the present writer on 2nd January, 1932, for pain in the lower abdomen of two days' duration with a history of having missed two periods, previous to which the periods were quite regular.

On examination, a painful swelling, small in size, was found in Douglas' pouch and on the right side of the uterus. Shortly after the examination, the patient collapsed, presenting all the signs of internal hæmorrhage. She was immediately operated upon, when a ruptured gestation sac in the right tube was discovered which was bleeding freely. Right salpingo-oophorectomy was performed. The patient made a good recovery.

The tube, on being opened, contained a gestation sac in which were two embryos of about 1½ months' development.

CONGENITAL DILATATION OF THE FETAL URINARY BLADDER

By PROBODH CHANDRA DAS, M.B.

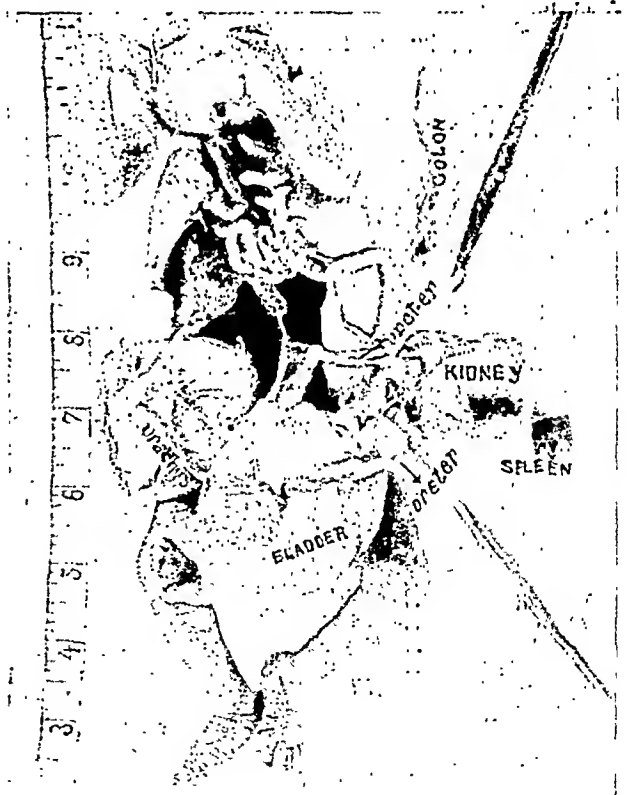
Calcutta, India

History of the case

THE patient was a Hindu Bengali, aged 30 years, a primigravida in her seventh month of pregnancy. The abdomen was tense and appeared like full term. Fœtal parts could not be made out nor the fœtal heart sounds heard. Excess of liquor amnii was diagnosed. The labour pains soon started and after a normal easy labour lasting about twelve hours the patient was delivered of twins. The first baby was an anencephalic monster with distended abdomen and the second one was a normal female. Both of them appeared to be of seven months' size. There was a moderate amount of post-partum hæmorrhage. After a stormy puerperium the patient was discharged cured.

Post-mortem examination

The foetus was an anencephalic monster measuring 12 inches in length and weighing



Photograph showing the various organs of the foetus. V, cut end of the vagina. Uterus and vagina have been removed to get a clear view of the bladder and the ureters.

3 pounds 14 ounces. The abdomen was distended, tense and felt like a cyst. Other external abnormalities noted were absence of anus and breasts. In the region of the external genitals, there was a fleshy protrusion, of about

1 centimetre in length appearing like a penis with a slight swelling underneath which looked like a scrotum. The protrusion was later found to be the clitoris.

The abdomen was opened and about 14 cubic centimetres of clear straw-coloured fluid was drawn out of the peritoneal cavity. The abdominal wall was very thin and measured not more than 3 to 4 millimetres. The bladder was distended to the size of a foetal head and was more or less ovoid in shape with a short bulging on the upper surface (see photograph). The distended bladder occupied the major portion of the peritoneal cavity. Both the ureters were slightly distended and tortuous, specially the right one. There was one kidney, the size of an almond, lobulated and hydronephrotic, and situated on the left side. Both the ureters opened into the same kidney. No supra-renal gland was found to exist. The urethra was absent and in its place was a very fine fibrous-looking cord proceeding towards the clitoris and ultimately blending with the surrounding tissues. Behind the bladder were the uterus and vagina, normally developed. The fallopian tubes and ovaries seemed normal. The colon ended in a blind pouch and was dilated and club-shaped on account of contained meconium.

The fluid in the bladder was drawn off with a syringe and afterwards an opening was made in the bladder to inspect its cavity. The wall of the bladder was thin, excepting the most dependent portion where it was slightly thickened. The lining surface was smooth but pale. No urethral opening was found.

Examination of the fluids

The fluids were odourless; no sugar, urea, phosphates, acetone, bile pigments or bile salts were present. Further details are given in tabular form below:—

	Peritoneal fluid	Fluid in the bladder
Amount	.. 15 cubic centimetres.	70 cubic centimetres.
Colour	.. Pale yellow	Clear.
Specific gravity	.. 1006	1008.
Reaction	.. Alkaline	Alkaline.
Deposit	.. Thick whitish	Nil.
Albumen	.. Present (slight)	Present (slight).
Blood	.. Present	Present.
Rivalta's test	.. Negative	Negative.
Microscopic examination.	Nil	A few red blood cells and pus cells

Review of literature

Goldberger (1929) collected from the literature 217 cases of congenital dilatation of the foetal bladder. Jeffcoate (1931) described a case making a total of 218 cases. It is evidently a rare condition especially as a cause of dystocia. For most of our knowledge on the subject we are indebted to Spicer (1908), who dealt with the subject exhaustively.

The children affected have been mostly males. Foetal ascites has also been present in a few

cases (Gupta and Das, 1931). The condition is often associated with other abnormalities, commoner ones being spina bifida, talipes, mal-developments of the genitalia, and defects of the lower alimentary tract. Imperforate anus is a more or less constant feature. The rectum is usually absent, the colon ending in a cul-de-sac. Schwyzer quoted by Dorland (1919) stated that dilatation of the Müllerian ducts (uterus and tubes) may be associated with vesical distension.

The conditions of the urinary tract have varied from moderate degrees of enlargement of the bladder with normal ureters and kidneys to great enlargement of the bladder with bilateral hydronephrosis. In some cases complete renal atrophy is noted and in other instances there may be total absence of a kidney and a ureter. The bladder generally retains its normal shape; but there may be present one or more loculi. The bladder wall in some of the cases is very greatly thickened and in others it is extremely attenuated. An extreme degree of vesical distension with dilatation of the ureters and renal pelves is the rule.

Ballantyne (1902) thinks that two different classes of case should be distinguished, the first, in which the bladder is distended alone; and the second in which it is hypertrophied as well as distended. Spicer, however, is not convinced that there is any necessity for such a distinction. He holds that hypertrophy and dilatation of the bladder can only arise where there is actual or virtual means of exit for the contained fluid.

Ætiology.—From the point of view of ætiology, these cases could be divided into two groups, namely: one in which some form of urethral obstruction is present, and the other in which no such abnormality of the urethra is present. The cause in the first group of cases is to be found in atresia, or complete absence of the urethra. Very often obliteration of the meatus urinarius or partial defect of the urethra is present; or the urethra is replaced by a mere cellular cord (Birnbbaum, 1912). According to Dorland imperforation of the urethra is almost invariably present, although in some cases this does not hold true, and then the occlusion of that canal is produced by a valve-like fold of the vesical mucosa.

For the ætiology of the second group of cases, many suggestions have been put forward. Among them may be mentioned hypo-æsthesia or hyper-æsthesia of the bladder. It is believed that in all probability the underlying cause is an abnormality in the neuromuscular mechanism.

The fluid.—It is always clear, limpid, serous, of low specific gravity (less than 1010), and of a light citron-yellow colour. It is more or less strongly albuminous and contains practically no urea. It varies in quantity from a few grammes to six or more litres.

The origin of the fluid is easily explained if the former view of regular discharge of foetal urine into the amniotic cavity is taken into consideration, in which case an atresia or an obstructed urethra will readily give rise to a distended bladder. But it is now accepted that the foetal kidneys normally do not secrete at all, or at most nothing but water in minute quantity, and even that only during the last few days before labour. The true renal function in intra-uterine life is carried on by the placenta and according to Spicer foetal kidneys secrete only when the placenta becomes defective as an excretory organ. Most foetal abnormalities, even of the gravest nature, are not incompatible with foetal life and growth. Naturally, therefore, atresia or absence of the urethra may readily exist and the foetus, nevertheless, advances to full term and post-natal existence without experiencing any inconvenience and without having any accumulation of fluid taking place in its bladder. Jeffcoate believes that there is a definite association between the occurrence of urine in the foetal bladder and prolonged labour. On the other hand it has been stated that labour is not an important factor in stimulating urinary secretion since babies born by Caesarean section before the onset of labour have, on a few occasions, micturated within a short time of delivery.

Thus it will be seen from what has been said before, the origin of the fluid in the bladder is still a matter of dispute and no one has so far given a satisfactory explanation. Spicer believes that accumulation of the fluid in the foetal bladder results from some obscure pathologic process the nature of which is not yet properly understood.

Terminations.—When fluid does accumulate in the bladder, Spicer finds that there are four possible terminations of the condition:

- (1) In the earliest stages, exstrophy of the bladder.
- (2) Urinary fistula at the umbilicus.
- (3) Distension and rupture of the bladder into the peritoneum.
- (4) Dilatation and hypertrophy of the bladder.

Obstetrical considerations.—The condition generally occurs in primigravidae and in the early child-bearing period. Multiparae of all degrees have also been affected. The labour is generally premature usually occurring between the 6th to 8th months of gestation. There is often an associated condition of oligohydramnios or hydramnios. In the majority of cases the presentation is vertex. The next most common is breech. But any presentation may occur, thus there are recorded cases of transverse, brow and face. Recurrence of the condition is rare.

Owing to the rarity of the condition the diagnosis is not generally made until the patient has been exhausted by prolonged labour and unsuccessful methods of delivery.

Treatment depends upon the degree of vesical distension. In minor degrees delivery is generally effected spontaneously or by simple traction on the presenting part. But if the enlargement is great then the foetal bladder must be perforated in order to effect delivery. According to Lynch (1906), the girth of the foetal abdomen which causes dystocia is usually 45 centimetres or more. It is interesting to note that dystocia has been observed only in half of the recorded cases (Dorland).

Rupture of the uterus has been noted on a few occasions.

Summary

(1) A case of congenital dilatation of the foetal urinary bladder is reported.

(2) The mother was an elderly primipara. Labour was premature but normal and natural. It was a case of twin pregnancy, one child being normal, and the other an anencephalic monster with the following peculiarities:—(a) Pseudo-hermaphroditismus-femininus, (b) absence of breasts, (c) dilatation of the bladder, (d) absence of the urethra, (e) presence of one kidney with two ureters opening into it, and (f) absence of the anus.

(3) The effect on labour in these cases depends upon the degree of distension of the bladder, dystocia arising only in case of enormous distension. There was no dystocia in the case reported.

REFERENCES

- Ballantyne, J. W. (1902). *Manual of Antenatal Pathology and Hygiene. The Fetus*. Edinburgh: William Green & Son.
- Birnbaum, R. (1912). *A Clinical Manual of the Malformations and Congenital Diseases of the Fetus*. (Translated by G. Blacker.) London: J. & A. Churchill.
- Dorland, W. A. N. (1919). *Amer. Journ. Obstet.*, Vol. LXXIX, p. 474.
- Goldberger, E. (1929). *Monatsehr. Geburtsh. u. Gyn.*, Vol. LXXXI, p. 253.
- Gupta, N., and Das, P. (1931). *Indian Med. Gaz.*, Vol. LXVI, p. 186.
- Jeffcoate, T. N. A. (1931). *Journ. Obstet. and Gyn. Brit. Emp.*, Vol. XXXVIII, p. 814.
- Lynch, E. W. (1906). *Surg. Gyn. and Obstet.*, Vol. III, p. 628.
- Spicer, J. E. (1909). *Proc. Roy. Soc. Med. (Obstet. Gyn. Sec.)*, Vol. II, Part II, p. 1.

SOME NOTES ON PLANOCAIN IN SPINAL ANALGESIA*

By J. FLETCHER ROBINSON, B.A., M.D.
F.A.C.S., F.R.C.S.E.

and

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DURING the last nine months, we have used planocain with unqualified success in about 600 cases. Planocain is put up by May and Baker and is very efficient for local and spinal anaesthesia in 1 per cent solution. The solution

* Paper read before the Mysore Medical Conference held in February 1933.

is prepared in double-distilled water; this is boiled, planocain added, and the water boiled again. A fresh solution is prepared for each day's work. The solution is lighter than the cerebro-spinal fluid. The specific gravity of these two fluids has been estimated, all determinations having been done at 27 degrees Centigrade. After three hours standing, the specific gravity of the cerebro-spinal fluid was 1,007 and that of planocain—1 per cent solution—1,001.

As soon as it is injected, the planocain solution diffuses throughout the spinal fluid. In three to five minutes the drug is fixed in the sensory nerves and complete anaesthesia and relaxation are obtained.

Pre-operative preparation

The patient is not usually starved, but is given his usual meals on the previous day. No preliminary purgatives are given. Sodium bicarbonate in drachm doses, given three or four times a day for three days, maintains the alkalinity of the blood. Tincture of digitalis (minims xxx), given the previous night and repeated early the next morning, protects the heart. Three grains of luminol by mouth given an hour before the operation keeps the patient drowsy during the operation.

Level of injection

The injection is made between the spinous processes of the third and fourth lumbar vertebrae for all except upper abdominal cases, when the injection is between the second and third lumbar spines. We do not inject higher for fear of injuring the spinal cord, though Janeseo and others have injected even between the cervical vertebrae.

Position of patient

The injection is made with the patient sitting. The position of the patient after the injection depends upon the height of anaesthesia required. For all operations below the umbilicus the patient lies flat on the table for three minutes and then the table is lowered to Trendelenberg's position. For all operations above the umbilicus, the patient is placed on the back and the table lowered immediately to the Trendelenberg position. In three minutes, the anaesthesia is complete.

Dosage

The dosage depends upon the site of operation, the expected duration of the operation and the size of the patient. By experience, we have found the following doses to give satisfactory analgesia :

- For all operations below the symphysis pubis, 4 to 5 cubic centimetres,
- for all operations below the umbilicus, 5 to 7 cubic centimetres,
- for all operations between the umbilicus and ensiform cartilage, 7 to 12 cubic centimetres, and

for those above the ensiform cartilage, 15.25 cubic centimetres.

The anaesthesia lasts for about ninety minutes. In cases where the operations are expected to be prolonged, the dosage is increased proportionately.

The advantages claimed for this solution are its cheapness, ease of handling, the few complications that have followed and the unqualified success in anaesthesia obtained in every one of our cases. Planocain is very much cheaper than novocain. The preparation is easy. The complications during and after operations have been few. Of all the drugs used by us, this has given us the best results. We have not had a single case of failure in anaesthesia. With the drug in 1 per cent strength, 4 cubic centimetres is the minimum and 20 cubic centimetres the maximum dose we have given. Two radical mastoid operations have been done using 20 cubic centimetres of the solution and placing the patient in an extreme Trendelenberg position. The quantity of planocain in these two doses is 3 grains and $3\frac{1}{5}$ of a grain respectively and this small dose is not likely to give rise to toxic symptoms.

COMPLICATIONS:

On the table

Fall of blood pressure is one of the dreaded accidents on the table and was a common experience with us before we started planocain. This fall has been combated by a preliminary intramuscular injection of 10 minims of adrenalin, or 1 cubic centimetre of ephedrine solution a few minutes before spinal puncture. These doses may be repeated during the operation, if necessary. Fortunately, 1 per cent planocain and the regulated dosages now used have made this complication very infrequent.

Respiratory failure.—This happens when large quantities are used for higher centres. The solution reaches the fourth cervical segment and paralyses the diaphragm temporarily and the patient does not breathe, although the blood pressure and the heart beats are normal. This is only temporary, but has to be watched. The patient is told to try to take long, deep breaths, he is aroused by being spoken to frequently, and in a few minutes the effect on the phrenic nerve passes off and normal respiration is re-established. If paralysis persists, a mixture of 7 per cent of carbon dioxide and 93 per cent oxygen is given by the closed method and this starts the respirations. In one of our cases we had to resort to artificial respiration with oxygen for about ten minutes before automatic respirations started.

Other complications are nausea, vomiting (particularly in upper abdominal cases), pallor, perspiration, nervous excitement and a feeling

of tightness in the chest; these are all temporary and are combated easily.

After operation

Headache.—This is a distressing symptom and may be transitory or may continue for even three or four days. The headache varies in different cases and is seen more commonly among nervous patients, particularly those of the educated class, but less often amongst the uneducated, but more hardy, ryot. This headache is supposed to be due to low cerebro-spinal pressure caused by leakage through the puncture in the theca. This low pressure removes the cushion-like support from the base of the brain, which in turn presses upon the basal veins resulting in anæmia of the brain causing headache. To combat headache, we carry out the following treatment in all cases of lumbar anæsthesia, the moment headache is complained of: We raise the foot of the bed 10 or 12 inches thus attempting to keep the lower end of the spinal canal empty to prevent further leakage. Intramuscular injection of adrenalin chloride, 10 minims, is also useful. Pyramidon in 10-grain doses, repeated in six hours, if necessary, relieves headache in many cases. In

one case, a second lumbar puncture gave instantaneous and permanent relief.

Temperature and rigor.—In some cases there are rigor and rise of temperature. This comes on two to six hours after the operation and the temperature drops abruptly in a few hours.

Acute dilatation of the stomach.—This sometimes occurs a day or two after the operation and it has given us more anxiety than any other symptom. The treatment consists in recognizing the condition and instituting immediate treatment. The patient becomes restless, with very feeble and frequent pulse, and pallor and distension of the upper abdomen with respiratory distress sometimes accompanied by vomiting of slightly greenish fluid. Treatment consists in passing a small-calibre stomach tube through the nostril, emptying the stomach of all its contents, gently washing with saline, and leaving the tube in place for drainage until the tonic of the stomach returns. The prone position is essential in all cases. One cubic centimetre of pituitrin given intramuscularly every three hours is a great aid. Rectal and intravenous salines are helpful in restoring fluid loss if much vomiting has occurred.

A Mirror of Hospital Practice

A CASE OF ENDOCARDITIS TREATED WITH POLYVALENT ANTISTREPTOCOCCUS SERUM

By R. N. CHOPRA, M.A., M.D. (Cantab.)

LIEUTENANT-COLONEL, I.M.S.

R. CHOUDHURY, M.B.

and

B. SEN, B.Sc., M.B.

(From the Department of Pharmacology, School of Tropical Medicine, Calcutta)

S. D., a Hindu female aged 25 years, was admitted under the senior author (R. N. C.) into the Carmichael Hospital for Tropical Diseases on 12th April, 1933, suffering from intermittent fever of a hectic type.

History of present illness.—The patient had a sudden attack of fever about 3 months before admission and had been getting it ever since. For the first month fever used to come every second or third day, but later it came on daily. During the second month she had suffered from alternating pains in different joints. There was no swelling of any joint and the pains subsided spontaneously. During the early part of the third month, she developed a rash on the body, which however subsided, but the fever continued as usual. She was treated outside the hospital for malaria, tuberculosis and 'B. coli infection' by different medical practitioners, but the fever could not be controlled.

The patient had previously always possessed good health. She has had 3 children one of whom is dead.

Condition on admission.—The patient looked ill and had an anxious expression. She was anæmic with a yellowish tinge of the skin. There was a daily rise of temperature to 103° or 104°F. with a chilly sensation but no rigor.

Physical examination revealed the apex of the heart in the 5th left intercostal space in the midclavicular line. There was no thrill but a soft systolic murmur was heard localized at the mitral area. Heart beats were irregular there being definite missing of beats at long intervals, showing partial heart block. The pulse rate varied from 60 to 80 per minute; pulse compressible, volume fair. Blood pressure was s/d -85/40 mm. of Hg. There was no cyanosis, dyspnoea, venous engorgement, œdema or petechial hæmorrhages. The lungs were clear, the abdomen soft and the liver and the spleen were not enlarged. Knee-jerks were normal and there was no urinary trouble. An examination *per vaginam* showed no pelvic abnormality.

Laboratory findings.—Blood—hæmoglobin 70 per cent, red blood cells—4,120,000, white blood cells—15,000. Differential count—polymorphonuclears—72 per cent, small mononuclears—21 per cent, large mononuclears—2 per cent, and eosinophiles—5 per cent.

No malarial parasites were found in the peripheral blood and blood culture for malaria was negative. The blood culture for bacteria was negative after 72 hours on two occasions. Wassermann reaction, Widal, Aldehyde and Antimony tests were all negative. Agglutination against *M. melitensis* was negative. Blood calcium and blood sugar were normal.

Urine.—There was no abnormality in the urine. A culture from a catheter specimen showed staphylococcus albus only.

Stools.—No ova or protozoa found; culture showed *B. pyocyaneus*.

Throat.—No hæmolytic streptococci found.

Electrocardiogram reports.—As the cardiac condition of the patient was peculiar electrocardiograms were taken at intervals. The results are given below:—

15th April, 1933.—P—R interval of 0.16 secs. which is probably a little high for Indians. T wave inverted. Slow heart rate possibly due to vagotonic action and myocardial degeneration.

24th April, 1933.—P—R interval 0.18 secs.; T wave flat but not inverted showing slight improvement in myocardial condition. Missing of heart beats clearly shown.

5th May, 1933.—P—R interval 0.18 secs.; heart rate 75 per minute. P wave normal size and contour. T wave upright, normal contour. Condition of myocardium shows improvement.

29th May, 1933.—P—R interval 0.18 secs. normal; P wave normal. T wave flat in lead II; R bifurcated in lead III. Indication—myocardial degeneration.

Treatment.—To start with, the patient was ordered absolute rest in bed and no medicine was given except a diaphoretic mixture, while preliminary investigations were being carried out.

After 4 days the pulse was observed to be getting slower and more intermittent. The patient was considered to be suffering from rheumatic endocarditis of a subacute type with partial heart block. She was put on sodium salicylate 15 grains 3 times daily but there was no effect on the temperature or pulse with this treatment after 7 days. Larger doses could not be given as the patient used to sweat profusely and feel depressed after administration of salicylate.

She was put on potassium iodide and liquor hydrargyrum perchloridum mixture which was continued for one week. For three days after this mixture was started there was no fever but the pulse remained about 60 and occasionally intermittent; the systolic bruit continued. On the fourth day she had fever again. For the next 3 days again there was fever, the condition of the pulse remaining unchanged. This was followed by a sudden sharp rise of temperature to 105°F. with a pulse rate of 68 per minute and the patient had to be given sponging and an iced saline per rectum. The iodide mixture was omitted and sodium salicylate gr. xv t.d.s. was started again. Next morning the temperature came down and the patient was in a collapsed condition; she was cold and clammy, temperature 96°F., pulse 50, respirations 24. She looked dazed and toxic, she was kept warm and stimulants were given. At this stage the patient started getting fits of unconsciousness resembling Stokes-Adam's Syndrome. As all the other treatments had failed she was given an injection of 10 c.cm. of polyvalent antistreptococcus serum intramuscularly. This improved her condition and the injections were repeated every other day till 60 c.cm. of the serum were given.

The temperature has remained normal since that time and the patient has felt better and has steadily improved. The pulse has also become quite normal in rhythm and is no longer intermittent. Later she was given hæmatinic treatment and after a prolonged rest in bed was allowed graduated exercises. She was discharged later.

Condition on discharge from the hospital.—Hæmoglobin 80 per cent, pulse 80 per minute, regular. Temperature normal. No symptoms. Apex of the heart—normal position, though a faint systolic murmur can still be heard. Skiagram showed no enlargement of the heart.

Remarks

1. The case was clinically one of carditis involving both myocardium and endocardium, chiefly the latter with partial heart block.
2. Although streptococci were possibly the cause, the septic focus being probably in the heart, they could not be isolated from the blood, throat, urine or elsewhere.
3. The treatment with sodium salicylate, atropine and potassium iodide appeared to do little good. The condition of the patient however started to improve rapidly after injections of polyvalent antistreptococcus serum. There was no rise of temperature after the first

injection. Whether the serum acted in a specific or non-specific manner is difficult to say.

A CASE OF HICCUGH CURED WITH APOMORPHINE HYDROCHLORIDE

By K. N. DUTT, L.S.M.F. (Punjab), L.O. (Madras)

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THE patient, a school inspector, consulted me with the complaint that he had been troubled with a hiccough for the past three days.

I gave him a hypodermic injection of apomorphine hydrochloride gr. 1/10 the same evening. Soon after the injection he felt slight giddiness and nausea. He fell asleep in an hour's time and awoke in the morning with his hiccough gone and apart from a few short attacks during this day he has had no further trouble.

A CALCULUS IN THE TONSIL

By S. C. SARKAR, M.B.

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A MAN, aged about 45, came to the hospital for the removal of a fish-bone from his throat. I introduced my finger and felt something hard in the tonsil but could not detect any fish-bone. I then introduced a pair of crocodile forceps, guiding them by my finger which I kept in position. I found a rent in the tonsil and that a foreign body was lodged inside this hole. I grasped one edge of the rent with a toothed forceps and tried to remove the foreign body. After several efforts I was successful and I found that it was a calculus about the size of a big pea, black in colour and very hard. The man was completely relieved after the operation.

Calculi in the salivary glands and ducts are fairly common but I can find no record of one being formed in the tonsil.

INSANITY TREATED BY SULPHUR INJECTION

By K. K. SEN, L.M.P.

Narhan, Darbhanga District

History.—A Hindu male, 25 years of age, suffering from insanity of manic-depressive type, was brought for treatment a few months after the onset of the disease.

The attack was reported to be the second one, the first having taken place about two years previously, and it only lasted for a short time.

There was no history of venereal disease or addiction to any intoxicants. There was no family history of insanity.

Physical examination did not reveal anything particular excepting that the patient was debilitated.

Treatment.—'Sulfosin-leo'—prepared freshly by rubbing 1 per cent sulphur sublimate in pure olive oil and dissolving it at a temperature of 100°C.—was injected deeply on the outer side of the thigh at the junction of the upper and middle thirds, according to the recommendation of Major J. E. Dhunjibhoy, I.M.S.

Dosage.—The first dose was 1 c.cm. and the drug was injected bi-weekly the dose being increased by 1 c.cm. at each injection.

The maximum dose injected, however, did not exceed 4 c.cm. as that amount was sufficient to produce the desired pyrexia.

General treatment.—Fresh and nourishing food, baths, fresh air, occasional injections of hyoscine gr. 1/100 with morphine gr. 1/4 and atropine gr. 1/100.

Progress.—The temperature used to rise to 102°F. to 104°F. within twenty-four hours of each injection.

Pain was severe at the sites of injections. Altogether six injections were given the maximum dose being 4 c.cm. and the man completely recovered.

A PENETRATING WOUND OF THE ANUS

By M. K. PILLAI, B.A., M.B., C.M. (Mad.)
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History.—Maung Hla Gyaw, a Burman male, was admitted into the Civil Hospital, Maubin, Lower Burma, on the 25th December, 1932, with a long piece of lacerated small intestine and omentum protruding through the anus, as a result of a fall earlier the same day from a paddy heap 14 feet high on to a forked stick, the kind used to support country carts.

Condition on admission.—Temperature 100°F., pulse 94 per minute. No flatus or motions passed since the accident. The wound involved the anus and surrounding skin. Two loops of the small intestine each about 1½ feet long, with a piece of omentum about 1½ feet long, were protruding through the wound and lying loose over the perineum. The gut was lacerated, gangrenous and offensive. On examination by the fingers, a gaping wound was felt on the right side of the rectum, extending into the abdominal cavity. The abdomen was tympanitic and tender. The patient was restless, and had a feeble pulse and all the symptoms of peritonitis.

Operation.—Under chloroform, the parts were thoroughly cleaned, the omentum excised, the gangrenous portions of the gut to a length of about 3 feet excised and an end to end anastomosis made. The sutured gut, with the omental stump, was then gently returned into the abdominal cavity and the wound packed with iodine gauze. The patient stood the operation well.

27th December.—

Morning

Temperature—subnormal 97°F., pulse 94 per minute.

Evening

Temperature—101.2°F., pulse 112 per minute.

Patient restless and thirsty.

Turpentine stupes to abdomen, pituitrin injections and glucose water to sip, were ordered. Wound cleaned and another plug put in.

28th December.—

Morning

Temperature 98°F., pulse 80.

Evening

Temperature 100°F., pulse 100.

Passed flatus during the night and at time of dressing. Patient quiet, abdomen less tender. Wound clean and healthy, but bled a little. Same treatment continued.

29th December.—

Morning

Temperature—96.4°F., pulse 78.

Evening

Temperature—99°F., pulse 98.

Passed flatus frequently, had one loose, yellow motion, free from blood. Tympanites less, abdomen slightly tender. Treatment same.

30th December.—

Morning

Temperature—96.8°F., pulse 98.

Evening

Temperature—99°F., pulse 98.

Passed 5 more small liquid motions—abdomen soft and not tender. The wound is healing, the rent in the rectal wall closing up. Patient complaining of hunger, but still fed on glucose water only.

1st January.—Temperature—normal morning and evening. Bowels open.

3rd.—Patient complains of hunger and weakness. Two cups of Horlick's milk given in addition to the glucose water.

6th.—Two cups of Horlick and one cup of cow's milk given. Slight discomfort after cow's milk, but relieved after a good normal motion.

9th.—Wound healing satisfactorily—abdomen quite soft and normal. Patient put on milk and rice conjee.

12th.—Slight discomfort after rice conjee, as the bowels were not quite free.

15th.—Bowels loose. Patient not strong—same diet with some stimulants.

19th.—Patient gaining strength, but bowels inclined to be constipated, relieved by liquid paraffin.

From this time he steadily improved and put on weight. The wound healed. He was put on ordinary diet, and discharged from hospital on 10th February, 1933.

The case is peculiar as the gut and omentum protruded through the anus, the anastomosis was done *in situ* and the gut pushed back into the abdominal cavity through the anus.

RECURRENT VOLVULUS OF THE SIGMOID COLON CURED BY COMPLETE SIGMOIDECTOMY

By F. C. FRASER

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District Medical Officer, Coimbatore

THE patient, a man of some fifty-five years of age, was admitted in the month of March for volvulus of the sigmoid colon. Abdominal section was performed by Lieut.-Col. Paton, I.M.S., and the volvulus reduced.

The patient was re-admitted again in the following October with a recurrence of the old trouble. Abdominal section was performed by myself and the volvulus again reduced. To prevent a recurrence of the twisting, the colon was stitched to the abdominal parietics. It was greatly hypertrophied and harboured a mass of constipated faeces which probably caused the volvulus. The patient gave a history of long continued obstinate constipation.

He returned again in the following March when I performed abdominal section for the third time within a year. The parietal adhesions had stretched the stitching having quite failed to do its work, so I decided the only procedure to carry out was to remove the whole of the sigmoid loop. This was done and owing to the enormous hypertrophy of the loop, an easy end-to-end anastomosis was performed. Six hours after the operation the patient started a profuse diarrhoea probably due to catarrh from retained decomposing faeces. In spite of this dangerous symptom, he showed no other disturbance and left the hospital two weeks later completely healed.

PERSISTENT LEFT SUPERIOR VENA CAVA

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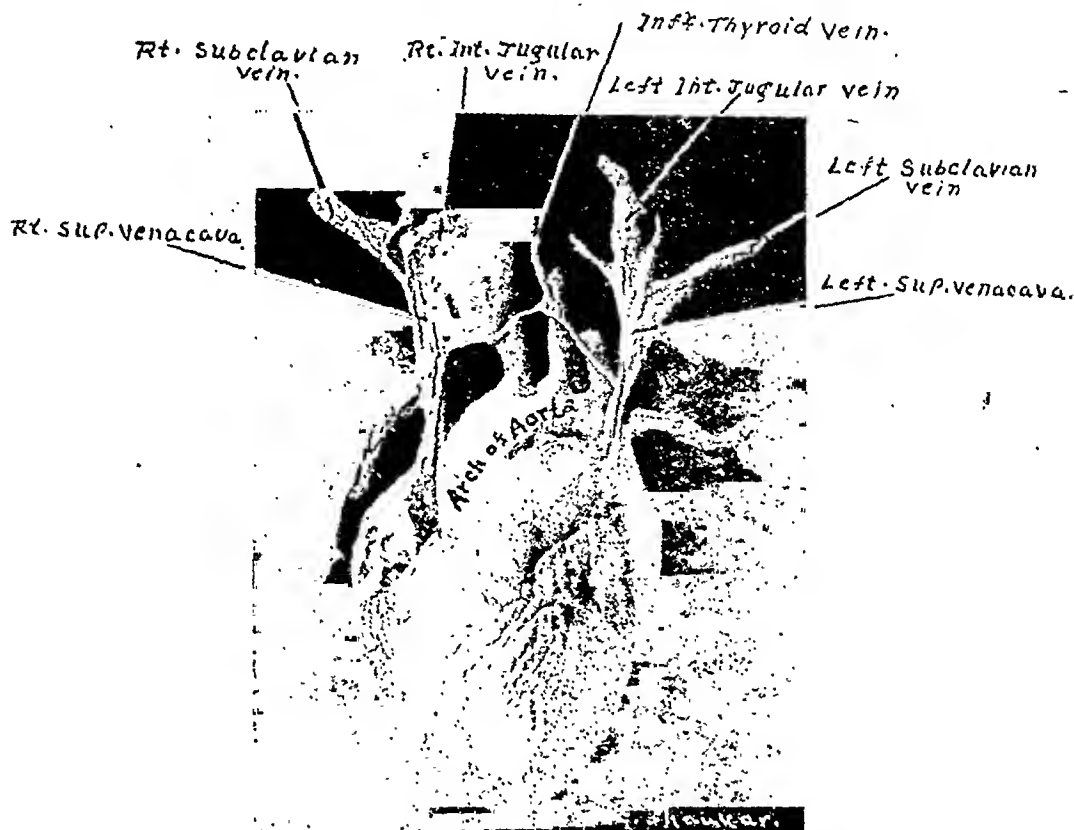
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THE persistence of two superior venae cavae is a rare occurrence.

The body of a male aged 35 (past history not known), dissected in the anatomical department of the Mysore University Medical College, presented a left superior vena cava in addition to the right. The left superior vena cava, formed by the union of the left internal jugular

with the left subclavian vein, descends vertically to the left of the arch of the aorta crossing the root of the left lung in front. It then turns to the right lying in the groove on the

condition described above, the transverse communicating branch is small, and the left primitive jugular and left duct of Cuvier have persisted and form the left superior vena cava.



Anterior view.

posterior aspect of the heart which is normally occupied by the great cardiac vein and opens into the right auricle independently. The right superior vena cava is formed normally and opens independently into the right auricle but is smaller in calibre. The left innominate vein which is represented by a small communicating vein between the two venæ cavæ receives the inferior thyroid veins.

In addition to its main tributaries the left superior vena cava receives the following veins :—

- (1) The left superior intercostal vein which receives a communication from the hemiazygos vein.
- (2) The thoracic duct.
- (3) The left internal mammary vein.

Embryological explanation

The right and left ducts of Cuvier receive the corresponding primitive jugular and subclavian veins and form the right and left superior venæ cavæ of embryonic life. A transverse communication forms between the two primitive jugular veins which later enlarges and forms the left innominate vein. The portion of the left primitive jugular, below the transverse communicating branch, atrophies and forms the upper part of the left superior intercostal vein, and the left duct of Cuvier atrophies and is represented by the vestigial fold of Marshall. In the abnormal



Posterior view.

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SEPTEMBER

CHOLERA AND BENGAL

ATTEMPTS are frequently made to estimate the amount in millions, or more often billions, of pounds that the existence of some particular disease costs the world. These estimates, which are seldom built on a very sound basis and are claimed only as the roughest of approximations at the best, are designed to impress hard-headed and hard-hearted business men to whom an appeal in the terms of the sufferings of human beings would mean nothing, and they probably serve their purpose, for even if the business man is inclined to accept them with reservation, knowing the methods by which they were made, they usually find favour with the politician—if they suit his purpose—and they certainly impress the readers of the headlines of the daily papers. Cholera in particular lends itself to this form of appraisal, as the dramatic rapidity of the course of the disease, which leaves little time for the victim to suffer, the high mortality, and the infrequency of any morbid scarring in those that recover, reduce the human suffering in connection with this disease to personal bereavement and to such conditions as are the direct outcome of economic loss if the victim happens to be the breadwinner of the household.

As far as the world in general is concerned the economic loss that is caused annually by the deaths of the tens of thousands of workers is unimportant in comparison to the enormous expenditure that is incurred on the organization for the prevention of the spreading of this disease. Port-health authorities in all parts of the world are continually kept on the alert to prevent the entry of the disease into their countries; and in the countries into which, despite this vigilance, it does find its way now and then, the public-health authorities have to maintain continuously a special organization for dealing with it. In every province in India the prevention and treatment of cholera is one of the most important functions of the public-health departments. Thus the expenditure that is incurred on account of the existence of this disease is distributed, practically speaking, over the whole world.

Now Bengal is held by the outside world to be the home of all cholera, and though there are undoubtedly other endemic foci in the world, the position of India both commercially and geographically makes this opinion regarding the responsibility of India in general and Bengal in particular in the matter of world cholera, virtually, if not actually, true. It is therefore

not surprising that everybody looks to India to do something towards ridding the world of this very expensive incubus. On the other hand it cannot be said that India has failed to realize her responsibility in this matter: every effort is made at India's ports to detect infected persons and to prevent them from leaving the country, whereas within the country itself the health departments of every province are continuously on the lookout for the first signs of the epidemic incidence of the disease; they have permanent organizations for actively combating it, and they take the most elaborate—and in recent years most successful—precautions to control the disease during *melas* and festivals, which in previous years were always the starting points of epidemics. Extensive studies into the epidemiology of the disease have been carried out by Russell, Rogers and Gill. Cholera has for years been high up on the list of diseases on which research is being conducted, and it was only the unfortunate financial crisis that prevented a large commission from being formed under the auspices of the Indian Research Fund Association to carry out a very complete investigation into this disease in all its aspects. That this commission never came into being and that its director-designate, Colonel F. P. Mackie, was allowed to retire and was thus lost to India was perhaps one of the most unfortunate sequelæ to the falling of the axe on the research organization in India.

There are at present four major enquiries being conducted on the subject of cholera in India, namely,

(a) a basic enquiry on the cholera vibrio, on its virulence, and on the virulence of the cholera-like vibrios under the Endowment Fund of the Calcutta School of Tropical Medicine and the Indian Research Fund Association.

(b) an enquiry into the antigenic structure of the cholera vibrio under the Indian Research Fund Association at the All-India Institute of Hygiene and Public Health, Calcutta.

(c) a bacteriophage enquiry under the Indian Research Fund Association at Patna.

(d) a bacteriophage enquiry in Shillong, also under the Indian Research Fund Association, combined with a field enquiry in Assam.

There is also an enquiry at the King Institute, Madras, and another in connection with the epidemiological bureau at Lahore. It can thus be said that India as a whole is not neglecting her duties in this matter, but is making a serious attempt to deal with the cholera problem.

If the world looks to India to do something about cholera, other provinces in India might very well turn to Bengal and ask what she, the cause of all the trouble, is doing about it. Bengal has a well-organized public-health department which has always made anti-cholera work one of her main activities; this department has a vaccine factory, makes and issues large quantities of vaccine, and each year carries out between one million and one million

and a half inoculations. Special arrangements are made for maintaining sanitary conditions at *melas* held within the province, and for pilgrim traffic, but the activities of the departments financed by the Bengal Government are directed mainly at holding in check the disease within the province and preventing its spreading beyond our borders. Were we to point the accusing finger at the Bengal Health Department and say 'How is it that during last quarter 40 per cent of the cholera deaths in India occurred in this province?', their answer would be simple; they would say 'Other provinces have only to prevent the entry of cholera, whereas we have it continually in our midst and every tank in Bengal is a potential source of infection'. This brings us to our point; all the measures that we have recounted above are merely palliative, but is Bengal doing anything to locate and to attack this source of the cholera of the whole world which lies somewhere within the province? There is at present research being done on cholera in Calcutta, but these researches are not sponsored by the Bengal Government. Bengal is a poor country, it may be said, it is no fault of her own that she is blessed with this unfortunate heritage which if it costs the world a great deal costs her more, she is finding it difficult enough to meet her actual financial obligations, and is not in a position to worry about problematical moral ones. But all activities are not necessarily expensive and Bengal could show India and the world that she is alive to her responsibilities in harbouring this undesirable inhabitant, by other means than by financing research workers.

It is suggested that a cholera committee should be formed in the province representing the Government executive, preventive medical organization, medical relief organization, and medical research. The committee should be of a semi-permanent nature, and it should be a small but strong one, so that though it did not possess executive powers there would be some chance of its recommendations being put into effect. Such a committee should collect the information that is available on the subject from various sources in the province, examine the results achieved by the various methods of cholera prevention at present in force, explore the possibilities of other methods which have been suggested by recent research work, and formulate a policy which would have as its final objective the banishing from the province of a preventable disease that has been endemic for more than twenty-five centuries.

The present methods of cholera prevention that are commonly employed are :—

Isolation.—This to be effective means the provision of suitable quarters and legislation to enforce their use. There is no doubt that the provision of hospital accommodation for cholera cases in the large towns in Bengal is a matter that admits of considerable improvement, but

isolation will never be applied satisfactorily in the rural areas and can therefore not be considered as a measure that is likely to achieve much by way of stamping out the disease.

Sterilization of water.—There is overwhelming evidence that cholera is mainly a water-borne disease and that wherever a wholesome water supply has been provided the disease has come to an end. It will be many generations before this can be achieved throughout the villages of Bengal, but it may be the eventual solution of the problem. However, spasmodic attempts at sterilization, such as the addition of potassium permanganate and chlorinated lime to wells and tanks, methods practised at present, are both costly and ineffective.

Preventive inoculation.—Anti-cholera vaccination has been employed for a number of years both in India and other parts of the world without any marked diminution in the incidence of the disease. It is important, therefore, that a proper assessment be made of its value in terms of incidence or mortality amongst the vaccinated population as compared with the unvaccinated, taking into account all the factors, whether environmental or the natural variations of the disease, which may influence such assessment. Before the efficacy of vaccination of man against cholera can be judged the following problems in active immunization must first be solved :—

(a) The danger, if any, of overlapping of inoculation and exposure to infection. This must be controlled by laboratory data.

(b) The assessment of the relative merits of the various types of vaccines in popular use and the mean duration of immunity conferred by different methods of protective vaccination.

(c) The value of active immunization in the light of recently acquired knowledge of bacterial antigens. The nature of bacterial antigen is one of the most important recent contributions to the science of active immunization and shows the necessity for a very close co-operation between the research laboratories and those engaged in the preparation of vaccines. It has been established that vibrios may so change in their antigenic properties (R and S; H and O variants) that they may become entirely without any protective value in immunization.

At the present moment a cholera vaccine is just a vaccine made from some strain or strains of cholera vibrios; the question whether it is made from a Bombay strain of cholera, prepared in France, and used in Calcutta, or whether it is prepared in Calcutta from strains that were isolated years ago and have been subcultivated under a variety of conditions ever since, does not appear to be considered.

Authoritative statements based on controlled field experiments together with laboratory controls on these points are necessary before the value of cholera vaccines at present in use can be judged.

Vaccination by bacteriophage lysates of vibrios, and other methods of inoculation might be considered; for example, the few animal and human experiments in the use of bacteriophage lysates of bacteria that have been reported have shown that there is a more rapid and a more solid development of immunity response with these lysates than with the ordinary types of vaccines. This is a method of immunization which owing to its simplicity and reputed efficacy deserves a trial.

Bacteriophage prophylaxis.—Experiments with bacteriophage in the prevention of cholera have been carried out by different observers, by d'Herelle in the Punjab, by Asheshov at Puri and in Behar, and Morison in Assam; the results appear to be encouraging, although they do not all bear close mathematical examination. It is not, in our opinion, a method that can be altogether dismissed, and it might be given a controlled trial in a small village area.

There are of course many other aspects of the cholera problem, but we will content ourselves with mentioning these few. There is in existence much organization for dealing with cholera, both from the preventive and from the medical relief point of view, and there are many research workers in the field, so that most of these problems could be tackled without introducing more organization or more research workers, if a committee could be formed on the lines suggested above to correlate the work of these various departments.

Medical News

'THE PRESCRIBER'

We have before now drawn our readers' attention to this useful Journal. In the May number there is a very complete review of the latest developments in endocrinology. Dr. D. M. Tudor contributes a note on incipient hypothyroidism in which it is shown how closely associated this condition is with many symptoms usually attributed to other causes. The various glands are dealt with in a series of up-to-date reviews, prepared by some half-dozen collaborators, bringing the knowledge of the subject down to April of the present year. In the case of the adrenal cortex, for example, there are four pages devoted to recent advances, to the anterior pituitary about three pages, and to the female gonads four pages. The endocrine products of the new British Pharmacopoeia receive special attention, and this issue of 56 pages of text is a complete review of the knowledge of the subject at the moment.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of September, 1883, Vol. XVIII, pp. 257 and 258)

ACCORDING to the most recent telegrams, cholera appears to be abating in Egypt, and it does not seem as yet to have made its appearance in Europe. At the time the mail of 3rd August left England, the total mortality caused by the disease was estimated at 11,600; some 80 deaths had taken place among British troops, including three officers. Surgeon-General W. G. Hunter, the late head of the Bombay Medical Service, had been deputed to conduct inquiries regarding the origin and spread of the epidemic. He was accompanied

by a band of medical volunteers. A scientific mission has, at the suggestion of M. Pasteur, been sent from France. It consists of four young doctors skilled in microscopic investigations, Drs. Roux, Thuillier, Straus and Nocard, and the special object of the mission is to search for a microbe whose discovery Pasteur anticipates with confidence.

The following interesting facts are culled from the Government resolution on Dr. King's reports on Cinchona Cultivation and Alkaloid Extraction for the year 1882-83.

The total number of cinchona trees of all sorts at the close of the year was 4,711,168, namely red (*Cinchona succirubra*) 3,713,200, yellow (*Calsaya ledgeriana*) 662,998, hybrid unnamed variety 304,378, and other kinds 30,592.

It is satisfactory to observe that the crop of the year is the largest that has yet been harvested on the plantations. It amounted to 396,980 pounds of dry bark, of which 372,610 pounds were of *Succirubra*, 22,120 pounds of *Calsaya* and *Ledgeriana*, and 2,250 pounds of hybrid bark. By far the largest portion of the produce was made over to the factory for conversion into cinchona febrifuge, while about 41,800 pounds of yellow and red barks were sent at the request of the Secretary of State to London to be there converted into various forms of febrifuge and returned to this country for trials by the Medical Department.

Dr. King has eventually succeeded in obtaining an analysis of the bark renewed on *Succirubra* trees that had their original bark removed by the shaving process introduced by Mr. Moens, the distinguished Director of Cinchona Cultivation to the Dutch Government. The results are thus described by Dr. King: 'The bark renewed rather slowly, but the analysis shows that it is very rich both in quinine and cinchonidine; and there can be no doubt that in countries where red bark trees are perfectly at home, and where their continuance in good health and vigour for a long series of years can be absolutely counted on, this shaving process must be a very excellent one.'

The price of the febrifuge was Rs. 8-8 a pound, and the percentage of the alkaloids extracted from the bark used in manufacture 2.73. The issues amounted to 8,901 lbs. 4 ozs. The issues to the public were 120 lbs. below those of 1881-82.

Current Topics

Atebrin in the Treatment of Malaria in Malaya

By SURGN. LIEUT.-COMMANDR. DAVID DUNCAN, M.B., CH.B., D.P.H., R.N.

(Abstracted from *The Malayan Medical Journal*, Vol. VIII, No. 2, June, 1933, p. 79)

SUMMARY AND CONCLUSIONS

THE medical organization at H. M. Naval Base, Singapore, is such that all Asiatics, whether employed directly by the Admiralty, or by the main contractors, or sub-contractors, are under strict medical control. They are medically examined on entry and during their sojourn on the Base a detailed history of each man is kept, all illness and treatment are recorded, and cases can readily be followed up after discharge from hospital.

During the past 15 months the writer has treated over 4,000 cases of malaria. Atebrin has been used for a period just over six months and over 400 cases have been treated with this drug.

Observations on the result of quinine treatment are made, and they correspond more or less to the general findings of workers who have used this drug in the treatment of malaria.

Atebrin is easily administered either in tablet, powder or liquid form. It leaves no lasting bitter taste in the mouth, and is therefore readily administered to children. It causes no deafness, ringing of the ears, photosensitivity, giddiness, anorexia, nausea, gastric upset, albuminuria, nor general depression. Cases under treatment in hospital are bright and cheerful. Patients are discharged to duty fit, and have not that lowered vitality which in the case of quinine treatment probably accounts in some degree for the frequency of relapses.

The fluorescent test for excretion of atebrin in the urine, faeces, and milk is not a satisfactory one unless the amount of atebrin being excreted is considerable. Atebrin is excreted in sufficient quantity in the urine to give a positive fluorescent test for from three to six days after treatment has ceased.

The optimum adult dose is 0.1 gramme or 1½ grains given three times a day for five days. Children even infants bear atebrin well, and to obtain good results the full dose suggested must be given.

Fifteen Asiatic women and forty-two Asiatic children were treated as outdoor patients. Atebrin was administered in full doses at various stages of pregnancy and no adverse effects were noted. Atebrin was administered to nursing mothers; it was found to be excreted in the mother's milk, and in one case was demonstrated in the infant's urine. None of the babies concerned showed any ill effects. Notes are given of a family of six children which were infected with benign tertian malaria which resisted all forms of treatment with quinine. Atebrin appears to have been somewhat more successful although it is too early yet to state whether the parasites have been finally eradicated.

The increase in the percentage of hæmoglobin in the blood during the course of treatment is in part due to rest and nourishing food. The persistence of the higher hæmoglobin index is noteworthy and satisfactory.

In benign tertian infections all parasites disappeared from the peripheral blood after 0.8 grammes of atebrin had been given over a period of two and a half days. In subtertian infection all asexual parasites disappeared from the peripheral blood after 1.0 gramme had been administered over a period of three days. There is a possibility that atebrin may have some delayed action on sexual forms as they were noted to disappear four or five days after treatment had ceased. Plasmoquin however gives more certain and quicker eradication.

In 93 per cent of benign tertian cases the temperature had dropped to normal within 44 hours and there was no subsequent rise. In subtertian infections the temperature dropped to normal in from 48 to 56 hours after the commencement of treatment. There was no difference noted in the temperature charts whether the case was treated with atebrin alone or in conjunction with plasmoquin.

The immediate effect on enlarged spleens during treatment was favourable. After an interval of some months 77.4 per cent of cases with splenic enlargement showed a marked decrease in the size of the spleen. This was also marked in the larger spleens.

Benign tertian cases treated with atebrin alone showed a relapse rate of 10.7 per cent. Benign tertian cases treated with atebrin given in conjunction with plasmoquin showed a relapse rate of only 5 per cent. It is doubtful whether in order to obtain this lower relapse rate one is justified in giving plasmoquin along with the atebrin in all benign cases. Subtertian cases treated with atebrin and plasmoquin gave a relapse rate of 3 per cent.

No toxic symptoms which could be attributed to the taking of atebrin have been noted. Discoloration of the skin has been seen in several cases. In no case where atebrin has been given alone have any abdominal symptoms been noted.

A general remark is made on the probable dangers of plasmoquin and of the necessity of exercising the greatest care when administering this drug.

Atebrin is a considerably cheaper method of treatment than quinine, from the view-point of the price of the drug, the saving in hospital costs and reduction in the time lost by the patient.

Undulant Fever

(Abstracted from the *Prescriber*, Vol. XXVII, June, 1933, No. 6, p. 217)

History.—The conditions known as undulant fever, abortus infection, and Malta or Mediterranean fever, while differing somewhat in character, appear to be varieties of the same infection, caused by different strains of the same organism.

For many years an infection of cattle, causing epidemic abortion in the animals, has been recognized. The causative organism was isolated by Bang in 1897 and named by him *Bacillus abortus*.

About forty years ago much trouble was caused in Malta by the prevalence of a certain kind of fever among the troops and the civilian population. This particular disease—first recognized during the Crimean War and known as Mediterranean or Malta fever—was found to be caused by an organism isolated by Bruce in 1887 and termed by him *Micrococcus melitensis*. In 1904 a British Commission investigated the causes of Malta fever and traced its origin to goats, whose milk was being largely consumed by the troops on the island. Removal of the goats and stoppage of the consumption of their milk completely stamped out the disease among the troops and greatly diminished its incidence among the civilian population.

Later it was observed that the incidence of Malta fever in goats was accompanied by frequent abortion among the animals, and in 1918 a certain similarity was shown to exist between *Bacillus abortus* and *Micrococcus melitensis*. A year or two later this similarity of the two organisms was confirmed, and in 1921 an important addition to knowledge of the subject was made when it was shown that *Bacillus abortus* may be present in the milk of cattle that have aborted, or even in that of carriers which have not aborted, and convey infection to human beings causing abortion in pregnant women.

In 1923 the identity of *Bacillus abortus* with the organism of Rhodesian undulant fever was established, and a year later it was shown definitely that the cow was the source of infection, and that in undulant fever the patient's serum was capable of agglutinating both organisms. Investigation soon revealed the existence in non-tropical countries of infection with *Bacillus abortus*, and while the symptoms did not in all respects tally with those of undulant fever as known in the tropics, the finding of the organism, and the application of agglutination tests, established the identity of the disease.

Bacteriology.—It is now generally held that *Micrococcus melitensis* is in reality a small bacillus and not a coccus, and the name adopted for it is *Brucella melitensis* (after its discoverer). The 'abortus' organism is regarded as a strain or variety—*Brucella melitensis* var. *abortus*.

Recent investigation has disclosed the existence of a number of varieties of *Brucella*. While these are usually referred to as if they were separate species, they are more correctly described as varieties or strains of the same organism. The more important of these are: *Brucella melitensis*, the caprine strain responsible for Mediterranean fever, *Brucella melitensis* var. *abortus* (bovine strain), and *Brucella melitensis* var. *suis* (porcine strain), these two being responsible for undulant fever. The porcine strain is much more pathogenic for man than the bovine strain; it seems to be more prevalent in America, while the bovine strain is more common in these islands. It is believed that cows may become infected with the porcine strain if

kept in proximity to swine. The various strains may to a certain extent be distinguished one from another by biochemical methods.

Etiology.—Infection by *Brucella abortus*, it appears, may reach the patient either by direct contact with animals harbouring the organisms—which seems to be common in America and on the continent of Europe—or by drinking the milk of infected cows, the more usual source of infection in Britain. It has been established that pasteurization of the milk completely destroys the organism and renders the milk safe for drinking. An investigation in Edinburgh only a year ago revealed the presence of *Brucella abortus* in about 35 per cent of samples of unpasteurized milk purchased in the ordinary way. In spite of this relatively wide distribution of the organism in milk, the actual number of cases recognized as undulant fever is comparatively small. This may be explained in two ways: first, many cases may be diagnosed as influenza and are not recognized as undulant fever; second, and more probable, individual susceptibility plays an important part and only a small proportion of these consuming abortus-infected milk are affected. The disease does not occur in epidemic outbursts among consumers of infected milk.

The portal of entry depends upon the manner of infection—in cases of contact with animals it may be through the skin, while with milk it is assumed that infection takes place through the alimentary tract. The tonsil has also been shown to be a possible route, and it has been suggested that the organism may settle and multiply there until the resistance of the host has been sufficiently lowered by fatigue or disease to permit its invasion into the blood-stream.

Symptoms.—Typical undulant fever is characterized by a series of febrile attacks, each lasting one or more weeks and subsiding into a period of absolute or relative apyrexia of uncertain duration. In his original description of Mediterranean fever, published in 1863, Marston remarked that no fever was so irregular as this in its course and symptoms. In the disease as it occurs in this country the type of chart varies, but the pronounced irregularities are characteristic. Sudden drops of temperature are accompanied by drenching sweats. In spite of the extreme irregularity of temperature, the characteristic evening rises followed by morning falls are usually seen. The duration of the disease is variable: it seldom lasts less than three weeks, more often six weeks or two months, and many cases are on record which lasted one or two years. The average severity of cases infected by *Brucella melitensis* is greater than that of abortus-infected cases.

Diagnosis.—As already mentioned, certain characteristic signs and symptoms are very helpful in diagnosis of undulant fever. The temperature chart is peculiar, the sudden drops of temperature are accompanied by heavy sweats, and the prostration of the patient is much less intense than would be expected from the temperature chart. Still the disease is liable to be mistaken for paratyphoid, influenza, etc., and diagnosis is often a matter of difficulty. For this reason laboratory diagnosis is of great importance, and in some cases is the only means of recognition. Several methods are available: (1) the agglutination test; (2) isolation of the organism from the blood or the excretions; (3) animal inoculation; (4) the intradermal test.

Agglutination test.—Without doubt the most valuable laboratory method of diagnosis is the agglutination reaction. This is usually given by the patient's serum after the second week of the disease, though sometimes it appears as early as the fifth day, and cases have been known in which the serum failed to agglutinate throughout the course of the disease. The test is performed by mixing graded quantities of the patient's serum with a killed suspension of *Brucella abortus*, incubating in a water-bath at 55°C. and reading the results after four and eighteen hours. The serum should be in various dilutions from 1:10 to 1:5,120.

Isolation of organism.—Cultivation of *Brucella abortus* from the blood or excretions is often possible, there being apparently a distinct relation between its presence in the blood and the patient's temperature—the higher the temperature the more probably will the organism be found.

Intradermal test.—Burnet's intradermal reaction consists in the injection into the skin of 0.5 c.cm. of a killed broth-culture ('melitene' or 'abortine') containing 500,000 organisms. A positive reaction is indicated by a red oedematous area at the site of injection, which persists for several days. Control injections are made in adjacent areas of skin. The test does not distinguish between the different varieties of *Brucella*, and for this reason the organism used is *Brucella abortus*. The method is simple, and frequently gives positive results where agglutination fails; on the other hand cases have been known to prove negative to the intradermal test where the agglutination titre was as high as 1:500. The test is not definitely specific, but is of value as a diagnostic in cases where no brucella agglutinins are present in the blood and when the organism cannot be grown on culture of the blood, urine, bile, or faeces.

Some American workers report a serological and clinical investigation of 100 persons exposed to infection through a known infected milk supply. Of these 22 showed evidence of active infection of the ambulatory subclinical type, 38 showed evidence of past infection, and 40 were not infected. None of the laboratory procedures employed was entirely specific; the intradermal test is regarded as being of distinct diagnostic aid. Laboratory findings, these workers conclude, are of extreme importance in the differential diagnosis of undulant fever.

Treatment.—At present no remedy is known to be specific for undulant fever, treatment being mainly symptomatic. Amidopyrine (B. P. 1932) has been found useful to combat headache and insomnia, while the pyrexia may be treated with antipyretics such as acetylsalicylic acid. In some cases intravenous injections of acriflavine (B. P. 1932) have proved of value, and several workers report good results from injections of S. U. P. 36. In America a vaccine has been placed on the market consisting of a saline suspension of killed organisms of *Brucella melitensis* var. *abortus* (bovine) and var. *suis* (porcine). Reports on its use are scanty, but on the whole they are favourable.

Zammit and Debono (Malta) report further developments in the preparation of a vaccine for the immunization of goats. Three years ago (*Prescriber*, 1930, Nov., 375) reference was made to their previous work when it was stated that while they had not achieved complete immunity they had succeeded in conferring a certain measure of protection in what is normally a very susceptible animal. They now say that they have elaborated a vaccine from a special avirulent strain of *Brucella abortus*, and that intradermal inoculation of goats with this vaccine is sufficient to protect them against the mild infection usual in these animals. These workers are confident that if the goats in Malta are treated as they suggest the spread of undulant fever might be effectually stopped.

A Note on the Uses of Glucose in General Practice

By F. O. TAYLOR, M.B., CH.B.

(From the *Practitioner*, Vol. CXXX, April, 1933, No. 4, p. 508)

THE general practitioner who has attended many families for some years knows from experience which of his young patients are prone to develop acidosis. As a rule they are of the nervous and delicate type, and readily go under to catarrhal infections. For some years, on the ground that alkali neutralizes acid, I tried to saturate these children's systems with bicarbonate of sodium, magnesium carbonate, and the like. But often vomiting was caused or increased; the temperature

remained high, the breath fruity; these symptoms show that, although there is not any demonstrable complication, the parents should be warned that some serious condition may be on the way. By slow stages, however, recovery would come, no doubt assisted to some extent by persistent alkaline medication. In passing, let me say that ammonium acetate has kept a high place in the purely medicinal treatment of juvenile sufferers from feverish complaints.

About eight years ago, after worrying for several days about the apparently serious condition of a child of 3 years of age who was maintaining a temperature of 102° to 104° F., without any obvious cause and with acidosis for which the usual alkaline treatment was given, I remembered that glucose was stated to be of value in such cases and promptly prescribed it. The temperature fell at once, and the child improved in an extraordinary way. Since then a load has been taken off my mind. If the acidosis is relieved but feverish malaise still persists, there must be some further complication.

Recently I attended a boy of 8 years with obvious acidosis. The administration of two heaped teaspoonfuls of medicinal glucose every two hours in water stopped his vomiting, cleared his urine, and removed the fruity odour from his breath, but did not bring down his temperature or stop some vague pain in the left upper epigastrium. I expected further developments. Eventually a basal pleurisy appeared.

Another small patient, always easy to treat for his chills and colds, one day did not respond to the usual measures; as a matter of fact he became seriously ill with only very vague abdominal pain. I sent the boy to hospital, where also he was treated as an obstinate case of acidosis; operation later revealed pneumococcal peritonitis.

Negative observations are as useful in some cases as positive findings; glucose cannot cure bacterial infections. As children grow, so does their liability to acidosis diminish. The adult simulates the condition with hyperacid urine and gastric secretion. But the fruity breath, in my experience, is usually associated with the acetonuria of diabetes, or with the terminal stages of dissolution.

As a valuable food, non-irritating, and easily absorbed, glucose is the only nutriment which I allow to adults during the rare cases of pneumonia I see nowadays. In hyperemesis gravidarum it can be freely used as a rectal meal with or without normal saline, and asthmatic children often derive great benefit from large quantities in addition to ordinary diet.

The Treatment of Acute Gonorrhœa in the Male

(Abstracted from the *Medical Journal of Australia*, Vol. I, No. 19, 13th May, 1933, p. 596)

ADVICE TO PATIENT

At the outset the patient should be warned as to the seriousness of his disease, that he must not give up treatment until assured of cure by his doctor. Half-hearted co-operation between practitioner and patient usually leads to bad results, and so as to insure the necessary co-operation, the patient should make frequent visits to the surgery. The patient should be particularly warned as to his mode of life; for any indiscretion during the course of the disease will most certainly delay cure. For example, any condition which tends to lower the resistance of the patient, such as keeping late hours, excessive smoking and indulgence in alcohol in any shape or form, cycling, riding on horse back, all forms of strenuous exercise are to be avoided, and sexual excitement must be debarred. No matter how good the local treatment, if the above-mentioned rules are not observed, results are indifferent, so that the patient's salvation lies largely in his own hands. Much has been written with regard to the prohibition of certain articles of diet, but experience has proved that

the ingestion of these foods has little or no effect on the course of the disease. The patient should be allowed good, wholesome food, including meat, otherwise his life will become a misery and thereby his natural resistance will suffer. He should be instructed to drink large quantities of water, which tend to correct the influence of irritating foods, and to micturate frequently, which serves the useful purpose of irrigating the urethra from behind. Attention should be paid to the bowels, and it is a good practice to order a good dose of opening medicine at the outset.

DRUG TREATMENT

No medicine as yet has been proved to be a specific for gonorrhœa, being merely prescribed for the alleviation of symptoms and sometimes as a placebo. For this purpose a simple mixture containing potassium citrate 1.2 grammes (20 grains) and potassium bicarbonate 1.0 gramme (15 grains) to 30 cubic centimetres (one fluid ounce) is useful, as is also a gelatine capsule containing sandalwood oil 0.6 mil (ten minims) and methylene blue 0.015 gramme (one-quarter of a grain), given three times daily. Particularly is this capsule useful in acute inflammation of the posterior urethra. Morphine 0.015 gramme (one-quarter of a grain), prescribed as a suppository, is sometimes necessary for the pain of acute inflammation of the posterior urethra.

VACCINES

Vaccines have largely fallen into disfavour in the treatment of acute uncomplicated cases of gonorrhœa, but have been universally used in cases with systemic involvement. Experiments carried out at the Rochester Row Military Hospital by Thompson and Lees in 1919 proved that, when large doses of detoxicated vaccine were used, gonococci disappeared from the discharge in less than half the number of days than in cases treated without vaccine. The administration of vaccine in acute gonorrhœa seems to be quite logical for the purpose of improving the patient's resistance. Detoxicated gonococcal vaccine is given intramuscularly into the upper and outer quadrant of the buttock in doses increasing from 2,500 millions to 10,000 millions, every fifth day.

LOCAL TREATMENT

The patient is instructed to procure a roll of cotton-wool, a packet of gauze, a tight suspensory bandage and also a small all-glass syringe with a blunt point. The wool is cut into squares and inserted on the inner surface of the suspensory bandage for the purpose of catching the discharge. Gonorrhœa bags and plugs of cotton-wool are not to be used, nor is anything to be tied around the penis, for by so doing drainage is interfered with. In patients with long prepuce a strip of gauze is placed over the glans penis and then the prepuce is pulled forwards. This dressing prevents the discharge from accumulating in the sulcus, thereby causing an infection of Tyson's glands, which are situated one on either side of the frenum.

The two methods of choice for local treatment are: (a) irrigation from douche can, (b) injection by small all-glass syringe. Most experts prefer the large syringe of 150 cubic centimetres capacity for irrigating purposes, but unless the operator is thoroughly practised in the technique of its use, more harm will be done than good. In general practice, therefore, the douche can method with special irrigating apparatus is to be preferred. This apparatus should always be kept in the surgery of the practitioner and be sterilized before use each day. The patient must not be allowed this method for home use, because of the possibility of introducing secondary infection.

For the purpose of injecting the urethra, a small all-glass syringe with a blunt point should be prescribed, and the physician should give instructions as to its use. The patient is allowed to treat himself at home by this method, injecting one of the organic silver salts which will later be described.

By the use of irrigating solutions we can only hope to destroy and wash away the organisms on the surface, together with the pus and mucus, thereby rendering the mucous membrane an unsuitable medium for the growth of bacteria. At the same time they promote drainage, and when used in suitable strengths create certain tissue responses. They are best prescribed in weak solution, and no good purpose can be served by prescribing them in strong solution, for the reason that they promote too much tissue response and thereby damage the tissues, sometimes beyond repair. The same can be said with reference to solutions for injecting the urethra by means of the small syringe.

Many antiseptics have been prescribed for the treatment of gonorrhœa, most of them proving their worth, but it is generally considered that potassium permanganate, used in a strength of 1 in 8,000 for irrigating purposes, is the most suitable. For injection of the anterior urethra, one of the organic silver salts is best prescribed, preferably protargol 0.25 per cent to 0.5 per cent and for the posterior urethra, argyrol 5 per cent.

In treating the urethra particular care must be observed in the prevention of trauma, which is the most common cause of complications. For the technique of irrigation and injection the reader is referred to the recognized textbooks.

The routine treatment of acute gonorrhœa of the anterior urethra consists in daily irrigation with potassium permanganate solution (1 in 8,000) and injection of protargol solution (0.25 per cent) two or three times a day as well. The solution must not be allowed to enter the bladder in the early stages. When the disease runs a normal course, this method of treatment is continued until the symptoms and signs disappear, with the exception that in the decline the number of injections is decreased. At every visit a macroscopic examination of the urine is made, for by this means one is able to follow the course of the disease, and also frequent smears from the discharge should be examined, the number of pus cells, epithelial cells, and the presence or absence of gonococci being noted. When many epithelial cells are noted in the smear, it means that the treatment is too severe.

It is bad practice to insert a sound, bougie, medicated or otherwise, into the urethra, in acute cases, or even to pass a soft catheter, except in acute retention of urine as a last resource. The treatment of acute gonorrhœa by means of medical diathermy, although never very popular, has fallen into disuse.

No mention has been made so far of abortive treatment, for the reason that, although it is obvious that the earlier the infection receives treatment, the shorter the duration of the disease, this result is obtained by the ordinary methods of treatment above described just as quickly and very often more effectively than by the more enthusiastic methods advocated.

When strong solutions are used in an attempt to abort gonorrhœa, the tissues are devitalized, and irreparable damage is done in the shape of infiltrations of the urethra.

Certain acute complications sometimes arise during the course of acute gonorrhœa, such as paraphimosis (which is treated by immediate reduction), intense swelling of the *glans penis*, abscess of Tyson's glands, and periurethral abscess, the latter conditions being treated by bathing with hot water or hot fomentations. Early incision of Tyson's abscess is recommended, otherwise it might rupture into the urethra and cause urinary fistula, but in periurethral abscess, incision is not resorted to until the abscess points on the skin surface. In hyperacute conditions it is advisable not to begin treatment for a few days.

One must always be on the lookout for the onset of posterior urethritis, which may happen at any time after the first few days. It is usually ushered in by the lessening or disappearance of the discharge, more or less urgent frequency of micturition, with varying degrees of pain at the end of the act, and perhaps the expression

of a few drops of blood. Frequently there are no symptoms other than that the urine becomes turbid; this explains the reason why it is so necessary to examine the urine before treatment. When the posterior urethra first becomes involved it is necessary to suspend all forms of local treatment, to advise rest and prescribe morphine, 0.015 gramme (one-quarter of a grain) suppository or oral treatment combined with hot sitz-baths until the acute symptoms disappear and the act of micturition becomes normal again. Then urethro-vesical lavage may be commenced, using potassium permanganate solution (1 in 8,000) or injecting 5 per cent argyrol solution into the posterior urethra by means of a small syringe. These manipulations must be carried out with the utmost care, and unless the practitioner is sure of his technique and is confident that he is not going to produce trauma, they should not be attempted, otherwise severe and long-lasting complications may arise. When the posterior urethra becomes infected, the prostate and vesiculae seminales frequently become involved, either mildly or sometimes severely. Acute inflammation of these organs is treated on the same lines as acute posterior urethritis. When abscess formation takes place, combined with retention of urine, immediate prostatotomy should be performed. Examination *per rectum* should never be performed whilst the disease is in its acute stage except for the purpose of detecting an abscess. When the acute and subacute stages have subsided, the disease becomes localized in certain areas, such as the Littre glands of the anterior urethra or perhaps the prostate gland or seminal vesicles. It then becomes necessary to eradicate the infection by means of dilating the urethra with curved metal sounds and topical treatment by means of the urethroscope, and also by massage of the prostate and seminal vesicles.

One is unable to lay down any set time for the cure of acute gonorrhœa, because it depends entirely upon the many considerations which have been described in this article.

NORMAL M. GIBSON, M.B. (Sydney).

Reviews

STARLING'S PRINCIPLES OF HUMAN PHYSIOLOGY.—Edited by C. L. Evans, D.Sc., F.R.C.P., F.R.S. Sixth Edition. London: J. and A. Churchill, 1933. Pp. xiii plus 1122, with 562 illustrations, 10 in colour. Price, 24s.

Starling's Physiology is probably read by more medical students than any other book on the same subject. To assimilate its contents from cover to cover—no mean task, as there are now over eleven hundred well-filled pages—is to ensure an easy passage through practically any examination on physiology.

This is the second edition since Professor Starling's death, the last edition appearing in 1930. Even in this short time, the work that has been done on the subject has necessitated very considerable changes and some of the chapters have been entirely re-written. A feature of this edition is the inclusion of a few select references; as the editor points out, these do not claim to be comprehensive, because there are 4,000 papers on physiological subjects published each year.

A special word of praise is due to the publishers for keeping down the price of this book to twenty-four shillings. It is very difficult to see how they have achieved this, as the book itself bears no signs of the exercise of the strict economy that must have been necessary.

It is not necessary for us to add any words of recommendation; it is sufficient to draw attention to the fact that a new edition of the best book in the world on physiology has been published.

SYNOPSIS OF SURGERY.—By E. W. Hey Groves. Tenth Edition. Bristol: John Wright and Sons, Ltd. Pp. viii plus 693, with 163 illustrations. Price, 17s. 6d.

For the past twenty-five years this book has had an established reputation amongst candidates preparing for examinations, and it may be safely predicted that the tenth edition will be as popular as its predecessors. The author has the gift of being able to compress the maximum amount of material into the smallest possible space consistent with completeness and assimilability, and his wide experience as an examiner has enabled him to give the student just what he requires.

In this edition the text has been brought up to date and, in parts, entirely re-written. Sections have been added dealing with the position of radium in the treatment of malignant disease, the surgery of the sympathetic system, and the Winnett-Orr treatment of bone sepsis. The temptation to include controversial matter has been resisted and conciseness has been achieved without making the text unreadable. To those who are able to profit from the use of a synopsis, this book can be recommended.

J. C. D.

INTERNAL DERANGEMENTS OF THE KNEE-JOINT.—By A. G. Timbrell Fisher. Second Edition, Revised. London: H. K. Lewis and Co., Ltd. Pp. xiv plus 205, with 120 illustrations. Price, 15s.

It is a matter of common experience to find a surgeon faced with obscure symptoms suggesting an internal derangement of the knee-joint, and torn between the possibilities of unnecessarily removing a healthy cartilage or dismissing a genuine disability with an injunction to 'paint it with iodine'. The subject has often been neglected in the past, and it is scarcely to be wondered at that some patients have sought relief from the quack and charlatan in the belief that the remedy lies in the application of some form of manipulative magic. As is pointed out in a preface by Sir Arthur Keith, the only form of curative magic is that founded on a thorough and accurate knowledge of structure, function and disease, and Mr. Timbrell Fisher has done a service in putting a complex and difficult subject on a scientific basis.

The second edition has been revised and partly re-written, with the inclusion of some original new matter. The book is attractively presented and the reproduction of the illustrations is excellent. It may be recommended to the general surgeon not only as a work of reference, but as an interesting book which can be profitably read in odd moments.

J. C. D.

DISEASES OF THE SPINAL CORD.—By Williams B. Cadwalader, M.D. London: Baillière, Tindall and Cox, 1933. Pp. xviii plus 204, with 72 figures in the text. Price, 29s.

Diseases of the Spinal Cord is an addition of considerable value to neurologic literature. In its range, it is comprehensive and thorough, and describes the various diseases that affect the spinal cord in all their aspects. The arrangement of the subject-matter and the grouping of the diseases show clearly an appreciation of the needs of the student and it is likely to stimulate a logical growth of ideas and an independent mode of thinking. A study of the essentials is a prerequisite to the knowledge of pathological processes and in no other branch of medicine is this principle more applicable than in the study of nervous disorders. The author has shown admirable judgment by discussing the anatomy and physiological functions of the spinal cord before proceeding to the nervous lesions. The neuron theory, the basis of all reasoning in neurology, the effects of degeneration, the reflexes and the reflex actions are all described from the view-point of physiologists. Syphilis of the spinal cord has been exhaustively dealt with. The treatment of nervous diseases is still in its infancy and therefore much light could be thrown on this part

of the problem. The author however does not claim too much for any one of the particular lines of treatment usually adopted.

The get-up is excellent. There are quite a large number of original photographs, and drawings of considerable value and artistic merit. The book will be very useful to neurologists and those interested in allied problems.

R. N. C.

PRACTICAL HAEMATOLOGICAL DIAGNOSIS.—By O. H. Perry Pepper, M.D., and David L. Farley, M.D. London and Philadelphia: W. B. Saunders Company, Ltd., 1933. Pp. 562. Illustrated. Price, 30s.

On picking up this book the reviewer received two mental impressions: one was that there was scarcely room in his library for another book of this kind, and the other that with so limited a scope the book must contain a great deal of padding. These first impressions were both wrong. The book is confined entirely to haematological investigations. Under each heading there is usually more than one method given, but there is no enumeration of all the possible, and impossible, methods just to fill up space; the methods are well selected, obviously by writers of practical experience.

Let us take as an example the chapter on the blood platelets; this covers 16 pages. The origin and development of the platelets has been discussed in a general chapter earlier in the book. Their physical properties, physiology and the mode of their destruction are detailed. There is a paragraph on the normal variations of this element of the blood; on this matter there are considerable differences of opinion and the conclusions of more than one observer have had to be given. Three different methods of counting platelets are given in detail. Then the variations from the normal, their significance and the artificially induced and diseased conditions, under which increases and decreases are found, are discussed. There is a section on the methods of increasing the count in the thrombocytopenic state; and finally a page is devoted to the differential platelet count.

The book is divided into three parts: the first is on the component parts of the blood, the methods of studying them and the significance of variations from normal; the second gives blood pictures in diseases of the haematopoietic system; and the third deals with the haematology of diseases that are not primarily diseases of the blood or blood-forming organs.

The book is well annotated, and there are a few very useful illustrations. It is a book that we can recommend to the haematologist.

L. E. N.

THE DIFFERENTIAL DIAGNOSIS OF ENDOCRINE DISORDERS.—By Allan Winter Rowe. London: Baillière, Tindall and Cox, 1933. Pp. x plus 220. Price, 23s.

THE science of endocrinology is of comparatively recent origin and is still in the melting pot. The ideas regarding the physiology and pathology of the various endocrine glands and their functions have not yet taken definite shape and every physician and specialist will admit the difficulty that so commonly arises in diagnosing and grouping the different endocrinopathies. Though voluminous literature has gathered on the subject, these are more of a theoretical than a practical nature, and consequently are not directly useful to the practitioner. Dr. Rowe has presented, in a systematic and concise way, the data collected during 20 years of intensive research in the course of which more than 5,000 individuals have been studied by a large group of clinicians and laboratory experts. The labour and energy involved in the execution is indeed enormous and Dr. Rowe is to be congratulated on this work.

The book is divided into three main sections: Section I deals with miscellaneous matters and clinical considerations including various methods of physical examination and history taking. Section II deals with

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all the chemical and biochemical changes encountered in endocrine disorders and contains a full description of individual methods to be adopted. This will be especially useful to all laboratory workers who would like to pursue the subject. In the assessment of the value of the various laboratory tests, the author has shown a keen sense of discrimination and breadth of view and has not allowed himself to be carried away to a diagnosis on the basis of one test alone. Section III deals with special examinations including clinical, laboratory and roentgenological procedures. The bibliography is well chosen and the book will strongly appeal to those practitioners who are interested in endocrine disorders.

R. N. C.

PSYCHOLOGY OF SEX.—By H. Ellis. London: William Heinemann (Medical Books), Ltd., 1933. Pp. xii plus 322. Price, 12s. 6d.

A CERTAIN amount of knowledge on sex psychology is now a necessity for the general practitioner, but it has been difficult to know where this knowledge may be acquired, because most of the smaller books that have appeared on this abstruse subject have been written by persons obviously not competent to carry out the task they have undertaken, and the larger books cover such a wide field that a busy practitioner or student becomes bewildered with the lengthy theoretical arguments, these books contain, and has not time to sort out, what is for him, the grain from the chaff. The result is that in all probability, after reading one of these advanced treatises, he will have a confused idea that all his patients are victims of repressions, many apparently quite harmless, and that if by suggestion he can turn these repressions into obsessions all will be well.

The *Psychology of Sex* is the type of book for which the practitioner and student have long been waiting, for within its three hundred and thirteen pages Havelock Ellis has condensed the essentials of his own much larger works as well as drawing on the continental writers on sex psychology, and he has produced a well-balanced presentation of the subject, which does not overemphasize the importance of a knowledge of sex in general medicine and which will give the student and the general practitioner all the information they are likely to need in the ordinary course of their work, but the possibility of more detailed knowledge being occasionally needed is catered for by the addition of a few references at the end of each chapter.

Prophecy is an unsafe practice in which to indulge as a general rule, but the reviewer feels he is on safe ground in stating that this book will be the textbook on this subject for English-speaking students and practitioners for many years to come.

P. A. M.

COLDS AND HAY FEVER. (MINOR MONOGRAPH SERIES).—By Frank Coke, F.R.C.S. London: Baillière, Tindall and Cox, 1933. Pp. x plus 148. Price, 5s.

THE common cold is one of the heritages of civilization. It is also a perpetual thorn in the side of the general practitioner, for most of the patients—or at any rate their mothers or aunts—have 'cures' which, if no better than those he himself can suggest, are seldom any more ineffectual. However, the physician is still expected to make suggestions for the prevention and cure of this most tiresome complaint, and he will find quite a number of useful hints provided in this book.

Hay fever is looked upon as rather a joke by everybody but the people who suffer from it; to these it may amount to a tragedy. It is funny to recount the story of the Harrow boy who sneezed sixty-seven times in succession, but when you have sneezed a thousand times in twenty-four hours you often feel more like making a violent departure from an unsympathetic world than joining the deriding laughs of your friends or listening

to the facetiae of your attending physician. In this matter also Dr. Coke has some useful suggestions and it is obvious that he at least does not underrate the importance of this condition when he suggests a course of treatment, which is to be carried out over a number of years before complete success can be expected. We notice that the author adopts the popular misspelling, 'wheal' for weal. It is a curious fact that h's always seem to give trouble—at the beginning of a word if you are hypo- and in the middle if you are hyper-educated.

A STUDENTS' MANUAL OF BIRTH CONTROL.—By L. C. Butler, M.R.C.S., L.R.C.P., D.P.H. Published by Noel Douglas. London. Pp. 39. Price, 1s. 6d.

THE fountain of books on birth control seems inexhaustible, and we must assume that the demand is the same. This particular book has points for recommendation. It is short, the author sticks to the point, and she is apparently orthodox. She is not dogmatic nor on the other hand too vague. Various birth-control methods are given in concise detail together with their advantages and disadvantages. The author might be accused of laying too much emphasis on the commercial aspects of birth control, as she gives the names and addresses of the manufacturers of appliances, etc., throughout the text, but we do not take this view and we consider that this particular practice adds to the usefulness of the book.

STREPTOCOCCI IN RELATION TO MAN IN HEALTH AND DISEASE.—By Anna W. Williams, M.D. London: Baillière, Tindall and Cox. Pp. xii plus 260. Plates 8. Price, 29s.

THERE are perhaps no other groups of bacteria that can claim such a volume of literature and such intensive study during recent years as those included under the genus streptococcus. This monograph contains a full and up-to-date account of the part played by streptococci in health and disease. The methods of isolation and studying the streptococci are fully dealt with. The work is of particular value because the author has devoted special attention to the subject for several years. A useful bibliography of the literature is appended.

There are unfortunately several mistakes in the text both in the style and in spelling and we cannot help feeling that the work would have been much improved if more attention had been paid to literary style. We hope that a very thorough revision will be made of this excellent book before the next edition. We can strongly commend this book to those interested in the very important genus of bacteria—the streptococcus.

C. L. P.

OTHER BOOKS RECEIVED.

1. *Woman's Periodicity.* By Mary Chadwick, S. R. N. London: Noel Douglas. Price, 6s.
2. *The Technique of Contraception—An Outline.* By E. M. Matsner, M.D. Published for the American Birth Control League, Inc., New York, by the Williams and Wilkins Company. Baltimore. 1933. Price, Re. 1.
3. *Qualitative Analysis.* By N. M. Shah. Published by The Students' Own Book Depot, Dharwar. Second Edition. Price, Annas 12.

Annual Reports

ABSTRACT OF THE ANNUAL REPORT OF THE DEPARTMENT OF PUBLIC HEALTH, YEAR ENDED 30TH JUNE, 1932. UNION OF SOUTH AFRICA

Malaria in Natal.—The malaria epidemic which occurred during the autumn was the worst yet experienced in Natal.

But disastrous as this epidemic has in many respects proved, there has yet emerged the fact that human communities are by no means helpless even in the most adverse climatic circumstances. Propaganda is gradually bearing fruit and communities that conscientiously carried out the simple precautions have escaped with little or no infection, while their neighbours suffered grievously.

The little Indian village of Umzinto escaped malaria, though surrounded on all sides by infection, and constantly traversed by vehicles bringing natives from badly infected areas to local doctors for treatment. The community is supervised by a voluntary Indian Committee employing an Indian trained in anti-larval work. A sluggish river passes through the village and numerous seepages everywhere provide ideal breeding-places. But every possible *costalis* breeding-place was visited once weekly by the trained Indian, who dealt successfully with all of them, as proved by results.

This instance is quoted as strikingly illustrating Professor Swellengrebel's reiterated assertion of the localization of the malaria vectors and the comparative simplicity of control. In essence, this amounts in Natal to making certain that every *costalis* breeding-place is found and dealt with once weekly.

In striking contrast with Umzinto were the conditions obtaining in the towns of Stanger, Verulam and Umkomaas, where the incidence of malaria was the worst of any in Natal towns. Systematic search for and treatment of breeding-places was not made. None of them employed a qualified inspector and the first two towns mentioned did not even avail themselves of the opportunity of sending an official down to the Government classes in Durban for training in anti-larval methods.

As examples of other communities that were kept virtually free of malaria as the result of well-supervised anti-larval methods may be mentioned the Umlhlanga Rocks Health Board and the Greenwood Park Health Board. Both of these had reason to be very well satisfied with the results of their efforts.

The sugar industry as a whole suffered less from malaria this year than in previous years. This again can be attributed very directly to improved anti-larval methods.

It cannot be too often reiterated that malaria is a local disease requiring to be combated by local measures which can usually only be effectively enforced by a properly constituted local authority thoroughly alive to the menace.

Transvaal.—In no part of the Transvaal did the incidence of malaria reach epidemic proportions.

The value of the drug plasmochin in rendering human carriers of malaria non-effective to mosquitoes is being investigated. The work carried out this season has demonstrated satisfactorily that the infective forms of the malaria parasite in man are destroyed by the drug when exhibited in suitable dosage. But the experiments have not influenced the infectivity rate of the mosquitoes in the area. This failure appears to be due to a very rapid turn-over of the mosquito population in native huts.

REPORT OF THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE FOR THE YEAR ENDED 31ST JULY 1932

This report is a record of continued expansion ever embracing a wider field of activities. Teaching has always been the chief function of the London School, and now even more time has had to be devoted to this side of the work on account of having three qualifying courses instead of two for the D.T.M. & H. The world-wide influence of this school is indicated in the tables on page nine showing that fourteen countries sent students during the year and over twenty-one countries

received these same students after their training; one came from Iceland and apparently returned there!

In the report of the division of clinical tropical medicine we note that '..... many natives suffering from different tropical diseases.....' The italics are our own, for it is a surprising thing to find a man of the long experience of tropical medicine enjoyed by the director of this division using a term of this kind. Surely in a report written in London the word native should be taken to apply to cockneys and we do not suppose this class were sufferers from the long list of tropical diseases cited as being available for demonstration during the year.

In spite of the many calls on the staff for teaching a great deal of research has been carried on, but in certain of the divisions notably those of bacteriology and immunology, biochemistry and chemistry, and epidemiology and vital statistics much of the work has no direct bearing on tropical problems. This of course does not detract from its value but is an indication that the London School is daily becoming a more important centre to the whole empire for the study of problems in medicine and hygiene.

As usual the division of medical zoology in all its departments, namely protozoology, helminthology, and entomology, presents a record of active research for the year.

The close connection the school has always had with India is still further strengthened by the appointment of Colonel S. P. James, I.M.S. (Retd.), as lecturer in the epidemiology of malaria, and the school is fortunate in having Sir Rickard Christophers, I.M.S. (Retd.), working in co-operation with the staff. Incidentally, Sir Rickard was not Director of the Malaria Survey of India, but of the Central Research Institute at Kasauli.

REPORT OF THE HEALTH ORGANIZATION FOR THE PERIOD JANUARY 1931 TO SEPTEMBER 1932. LEAGUE OF NATIONS, GENEVA. OFFICIAL NO. A. 28. III

Malaria Commission

EARLY in 1931, the Malaria Commission had to deplore the death of its Chairman Professor V. Ascoli, and Dr. Lutrario, who had been Chairman until 1930, was asked to take his place. Professor G. Bastianelli, Director of the Advanced School of Malariology, Rome, and a member of the Health Committee, was elected a member of the Commission in June 1931.

The Commission has continued its study on the efficacy of anti-malaria medicaments which might be prescribed instead of quinine, the present price of which constitutes a serious obstacle to the treatment and prevention of malaria. Of these medicaments, the Commission recommended the secondary alkaloids, mixtures of alkaloids and the total alkaloids of cinchona. After a consultation of experts held in London on 16th January, 1931, the Commission met at Geneva on 5th and 6th May to consider the standardization of the total alkaloids and mixtures of alkaloids. It proposed that the name 'Quinetum' should be reserved for a preparation consisting of quinine, cinchonidine and cinchonine in equal parts, that being approximately the normal proportion of these alkaloids in *Cinchona succirubra*, and the name 'Totaquina' for a new standard preparation containing the total alkaloids of cinchona. This preparation should contain at least 70 per cent of crystalline alkaloids, of which not less than 15 per cent must be quinine. Amorphous alkaloids should not, however, exceed 20 per cent, mineral matter 5 per cent and water 5 per cent. This new formula was communicated to the Commissions of the National Pharmacopœia in the different countries.

In September 1930, the Malaria Commission reached the conclusion that a conference of representatives of the governments of malarial countries should be contemplated with a view to determining those countries' real requirements in quinine and discussing

measures likely to reduce the price of the medicament so as to make it available for all malarial countries. The Secretariat was accordingly requested to collect from malarial countries documentation relating to the total number of malaria cases, the number treated, and the amount of quinine and secondary alkaloids of cinchona imported and distributed annually during the last ten years. This enquiry began in January 1931 and, up to the present, no less than ninety-six countries have forwarded their replies.

The international courses in malariology instituted in 1926 under the auspices of the Health Organization were held in 1931 in Paris, Rome and Hamburg, and the Health Organization offered nineteen scholarships to medical men from twelve different countries. In 1932, these courses were held in Paris and Rome, and twelve scholarships were awarded to medical men in twelve countries. Both in 1931 and in 1932, the field work which followed the theoretical instruction was carried out in Spain, Italy and Yugoslavia.

At the request of the Siamese Government, Dr. L. Anigstein, a member of the Malaria Commission, conducted an enquiry from 15th January to 27th April, 1931, into malaria and anophelines in Siam. His report was published in No. 2 of the *Quarterly Bulletin*.

On returning from his tour in China, of which a summary is given below, Professor M. Ciuca, Secretary of the Malaria Commission, visited in turn Indo-China, Malaya, the Dutch East Indies and Ceylon for the purpose of studying the anti-malaria organization, training of staff, epidemiological conditions and quinine requirements in those countries. His mission was greatly facilitated by the kind assistance he received from those responsible for the health services and anti-malaria organizations in those countries.

In Indo-China, which he visited at the invitation of the Governor-General, an inspection of the Pasteur Institutes at Saigon and Hanoi, with which the Anti-Malaria Service is connected, enabled him to secure information as to the general plan of campaign, the methods adopted and the work done by the entomological and epidemiological branches of the Anti-Malaria Service. Under the guidance of Dr. H. Morin, Director of the Anti-Malaria Service, he visited the red earth region of Cochin-China—which, in spite of its extreme fertility, has earned the name of 'the accursed lands', owing to its devastating epidemics of malaria—the cinchona plantations of the Pasteur Institute and the malarial zone of the Tonkin mountains.

In Indo-China, the *A. maculatus*, *A. minimus* and *A. aconitus* must be considered as carriers. The campaign conducted by the Anti-Malaria Service has achieved rapid success through the combined action of quininization, both preventive and therapeutic, and measures directed against the carrying species of anopheles—e.g., subsoil and open drainage, the abolition of water collections, oiling. Thanks to the results already obtained, the area in which the anti-malaria campaign is being pursued is continually increasing; the local authorities show a new spirit and spontaneously request the Anti-Malaria Service to undertake sanitation work of which they will bear the cost.

At the Hanoi Medical School, Dr. Ciuca was invited to open the first course in malariology organized by the Anti-Malaria Service. The work of the League of Nations Malaria Commission and the principles of the anti-malaria campaign with reference to local conditions formed the subject of this first lesson. It is intended to extend this course next year, so that other malarial countries in the Far East may profit by it.

Subsequently, Dr. Ciuca visited Singapore, Penang and the Malay States. His work was greatly facilitated through the good offices of the Director of Health and Medical Services in Malaya, Dr. C. J. Wilson. The *A. maculatus* is chiefly found in the hill district, whereas in the collections of brackish water in the coast zone the *A. ludlowi* may be a dangerous carrier. In Malaya, the campaign against malaria is directed against the carrying species in its larval stage. A protective zone

is established around groups of dwelling-places, after the breeding-places of the larvæ have been eliminated through drainage of the soil, either permanent or temporary in character, according to local conditions. At Kuala Lumpur, Dr. Ciuca was able to collect information concerning an attempt at mass prophylaxis by means of plasmoquine carried out on 300 coolies of a rubber plantation by Dr. A. N. Kingsbury, Director of the Institute for Medical Research.

In Java, under the guidance of Dr. Soesilo, Head of the Anti-Malaria Service, Dr. Ciuca studied the central anti-malaria organization, the training of staff, the methods of the anti-larvæ campaign, the cinchona plantations and the quinine factories. The *A. ludlowi*, the breeding-places of which extend all along the coast, is here the chief carrier; in the mountain region the *A. maculatus* and *A. aconitus* are found and transmit malaria up to an altitude of 1,200 metres. Near Batavia, Dr. Ciuca was able to examine the sanitation work undertaken under the direction of Professor Walch according to an original biological method in the enormous fishponds at Passerocean. The principle adopted is the destruction, through partial and periodic drainage of these ponds, of the floating weeds which constitute the breeding-places of the *A. ludlowi*. The results of this work are seen in a heavy decrease in malaria, the spleen rate in the neighbouring villages having fallen from 68 to 7, 5, 2 and even 0.

In Ceylon, under the guidance of Mr. Carter, entomologist, Dr. Ciuca studied the central and local organizations of the anti-malaria campaign. The setting up of an entomological service in 1921, under Mr. Carter's direction, made it possible to prepare a malaria chart of the island where infection is due to the presence of *A. culicifacies* and *A. listoni*.

Opium Commission

The 1925 International Opium Convention laid upon the Health Organization a twofold duty:

(1) To exempt from the measures of international control set up by the Convention preparations which, while coming within its scope owing to their composition, are not liable to give rise to the drug habit (Article 8), and

(2) To bring within its scope narcotic drugs to which it does not yet apply but which present the same dangers as those drugs which it has placed under control (Article 10).

With regard to the first of these tasks, the Health Committee concluded its examination of the lists of preparations which the Governments of the Argentine, Austria, the United Kingdom, Bulgaria, Estonia, France, Germany, Hungary, India, the Irish Free State, Latvia, Poland, Roumania, Siam, the Union of South Africa, the Sudan, Sweden and Switzerland had proposed to exempt from the provisions of the Convention, and a recapitulatory list of all the preparations thus exempted was published (document C.114.M.54.1932. III).

The Health Committee also continued the work involved by Article 10 of the Convention, and brought within the scope of the latter:

(1) A new narcotic drug: acedicone (acetylodemetlylodihydrothebaine) together with its salts, and the preparations containing it;

(2) All those substances enumerated in Article 1, paragraph 2, group I, of the Convention for Limiting the Manufacture of Narcotic Drugs which were not yet covered by the 1925 International Opium Convention.

Continuing its work on the standardization of the methods of ascertaining morphine content in the various opiums, which was referred to the Health Committee in 1931, the Commission of expert pharmacologists, under the chairmanship of Professor L. van Itallie, of Leyden, held its second session at the Hague, 11th to 14th July, 1932.

Before proceeding to the codification of a standard method, the experts thought it necessary to carry out

researches regarding a new method worked out by Professor Eder, of Zurich, and also the method based on the British Pharmacopœia, recommended by Professor van Itallie.

The Commission also drew up a scheme for the investigation of the standardization of methods of ascertaining the cocaine content of coca leaves. This scheme will be submitted to the Health Committee at its next session.

The Commission hopes to conclude its work in the spring of 1933.

At the request of the Advisory Committee on Traffic in Opium, the Health Committee undertook to study modern methods for the treatment of drug addicts in the various countries. An interim report was prepared by Dr. P. Wolff, of Berlin.

The Permanent Central Opium Board asked for the Health Committee's opinion on a new method of estimating the consumption of narcotic drugs. The study of this method, by which the total consumption of opiates is expressed in the number of average doses per head of the population, instead of in milligrammes of raw opium, was referred to a group of experts whose work is still proceeding.

Commission on the Fumigation of Ships

Influenced no doubt by the increasing importance of the fumigation of ships from the international point of view, owing to the provisions of the International Sanitary Convention of 1926 coming gradually into force, the Health Committee, in consultation with the Permanent Committee of the Office International d'Hygiène Publique, set up in the spring of 1928 a Commission on the Fumigation of Ships.

The first meeting of the Commission took place in Paris on 14th May, 1928, under the chairmanship of Surgeon-General H. S. Cumming. It drew up a programme of work and accepted with gratitude its Chairman's offer to organize experiments with regard to the fumigation of vessels by means of hydrogen cyanide in order to determine more exactly the value of this process, particularly in respect of:

(a) Its efficiency to destroy rats with the cargo *in situ*;

(b) The effect of the gas on different cargoes;

(c) The question of pocketing; and

(d) The influence of temperature, humidity and like matters.

At a plenary meeting of the Commission in May 1929, the chairman presented an interim report which summarized the replies he had received in response to his request for information on the methods of fumigation in force and the results achieved in the principal ports of the world, and suggested a programme of experimental work, which was approved.

In September 1931 a committee of experts composed of Dr. H. F. de Bruyne, Chief of the Disinfection Service, Rotterdam; Dr. W. Dreyer, Port Health Officer, Bremen; Dr. T. W. Monier-Williams, of the Ministry of Health, London; Dr. P. G. Stock, of the Ministry of Health, London; Dr. Ch. Vigne, Chief of the Port Sanitary Service, Havre; Dr. A. Vila-Rodriguez, of the Port Health Station, Cadiz; Dr. C. L. Williams, of the Quarantine Station, Staten Island, New York, investigated the work carried out in the United States on behalf of the Commission. The experts visited New York, Washington and Baltimore, where the Federal authorities had arranged for their benefit a number of demonstrations on the fumigation of ships by the various methods employed in the United States.

They were particularly interested in visiting the quarantine stations, warehouses and shipbuilding yards, and had an opportunity of discussing with the officials of those establishments the various aspects of fumigation: efficiency and dangers of the various methods, disadvantages of certain fumigants for the cargo, rat-proofing, the preparation of ships for fumigation, methods of ventilation, etc.

At the conclusion of their visit, the committee of experts drew up a report reviewing the practical investigations carried out by the United States Public Health Service, and indicating how far the results obtained provided answers to the questions set out in the programme drawn up by the Commission on the Fumigation of Ships.

This report was discussed in detail at a plenary meeting of the Commission in April 1932, and the reader will find the Commission's conclusions in No. 2 of the *Quarterly Bulletin*.

Leprosy Commission

A Conference on Leprosy, organized by the Leprosy Commission of the League of Nations, was held at Bangkok in December 1930 during the Eighth Congress of the Far Eastern Association of Tropical Medicine. Its report was published in document C.H. 970.

The members of the Commission were also invited to attend the Conference on Leprosy of the Leonard Wood Memorial for the Eradication of Leprosy held at Manila in January 1931. The report of this Conference was published in English in the *Philippine Journal of Science*, Volume 44, No. 4, April 1931, and in French in the *Revue d'Hygiène*, Volume XLIV, No. 6, 1932. While the report drawn up by the Leprosy Commission at Bangkok lays down the general principles of prophylaxis, the report of the Manila Conference contains technical conclusions and information. Both state that greater uniformity should be introduced into the study of leprosy. The standardization of treatment presents very great difficulties. The first step in this direction would be to introduce systematic comparisons, such as are already made by several institutions dealing with leprosy. A beginning might be made by:

(1) Comparing two equivalent groups of subjects placed in the same circumstances, one only of which would receive treatment by chaulmoogra;

(2) Making a further experiment of the same kind to determine the value of intradermal injections;

(3) Analysing observations on a sufficiently large number of patients who have undergone continuous treatment, grouped according to the form of the disease, its gravity, etc., with a view to obtaining information as to the conditions of and reasons for the success or failure of the treatment;

(4) Formulating those methods for the preparation of oils and esters which are recognized to be most satisfactory.

In April 1931, the Brazilian Government made an offer to the Council of the League to establish an international centre for research on leprosy under the auspices of the League at Rio de Janeiro. This centre was to be legally separate from the League and entirely autonomous, the Brazilian Government undertaking to bear the whole cost of maintaining and working the centre. The League accepted this offer, and the centre, with a representative of the League of Nations, a representative of the Argentine Republic and a representative of Colombia will sit on its governing body.

ABSTRACTED FROM THE ANNUAL REPORT OF KASHMIR MEDICAL MISSION OF THE CHURCH MISSIONARY SOCIETY FOR THE YEAR 1932

THIS report gives a record of strenuous work for the year 1932. This hospital is of special value because it brings the people of Kashmir into touch with skilled medical and surgical assistance. The following figures indicate the amount of work done by this hospital during the year:

There were 20,771 new out-patients, with a total attendance of 50,453, and the in-patients numbered 2,199. In addition to the work at headquarters certain members of the staff go on tour from time to time and in this way treat many persons who are not or cannot be attended to in government dispensaries. Subscriptions to this deserving charity may be sent to Dr. E. F. Neve, Mission Hospital, Srinagar, Kashmir.

ABSTRACTED FROM THE BRITISH GUIANA
MEDICAL ANNUAL FOR 1932. TWENTY-FIFTH
YEAR OF ISSUE

The major portion of the book is devoted to clinical and pathological records of cases of special interest occurring in the various hospitals in the colony. All of these papers might be read with advantage by tropical practitioners anywhere in the world as they are essentially practical in character.

The latter portion of the annual gives a full record of the British Medical Association meetings in British Guiana which is followed by a number of abstracts of papers read at some of these meetings.

The small book is of handy size and it is bound in stiff card-board which makes it easy to hold and therefore all the more pleasant to read, and it is also printed on remarkably good paper for a publication of its nature.

ABSTRACTED FROM THE ANNUAL REPORT OF
THE KING EDWARD VII SANATORIUM,
BHOWALI, UNITED PROVINCES, FOR THE
YEAR 1932

This sanatorium which was established in 1912 by the people of the United Provinces of Agra and Oudh for the treatment of early cases of pulmonary and laryngeal tuberculosis, continues to do valuable work as is indicated by the annual report for 1932 which we have just received.

On account of its altitude and the intense cold in winter the sanatorium is only open from March to December each year, but even so, with accommodation for 'nearly 110' patients, the returns show that 180 cases were dealt with in 1932. This is not a free institution except for a very few patients but the scale of fees payable is small. At the end of the report the rules, scale of fees, how to obtain admission, etc., are given in full.

'NURSING EDUCATION AND SCHOOLS OF
NURSING' (METHODS AND PROBLEMS OF
MEDICAL EDUCATION) 21ST SERIES. PP. 226.
ILLUSTRATED. PUBLISHED BY THE ROCKE-
FELLER FOUNDATION. 1932

This is an arrestingly interesting account of nursing education in various countries, including America, Canada, China, Denmark, England, Finland, France, Hungary and Siam. It gives a wealth of detail of the actual methods of training nurses, and of post-graduate study, in which America and Canada are particularly progressive, of the problems and difficulties which arise owing to the combination of a great amount of theoretical study with the actual nursing of the hospital wards, of financial difficulties which arise and the means available to meet them.

In America and Canada great stress is laid on the importance of a university training for nurses in conjunction with the general hospital training, pre-graduate or post-graduate. To quote from the opening article (Yale University School of Nursing) 'the importance of University relationship cannot be over-emphasized for it has made possible within a comparatively few years an evolution of the programme of nursing education that could be realized only through the freedom for study, experimentation and demonstration that such a relationship permits'. In the second article (Cook County School of Nursing, Chicago) 'the alert, sensitive, refined type of woman needed to serve in the various fields of nursing, in which she often carries the responsibilities of life and death, is more apt to be found at a University securing her education'.

The impression received on reading the various articles, particularly those from America and Canada, is the great consideration for the nurse or student during her training, and the absence of methods which prevail in many older hospitals where the primary object is the achievement of the daily ward work, without due consideration for the thorough training of the nurse.

In hospitals, where understaffing is so prevalent, the training or 'nursing education' of the nurse has often to be a secondary consideration. It would have been interesting if the ratio of nurses to patients, during the training of nurse-students in America and Canada had been included; the question presents itself to a practical mind as to when the actual nursing of the patients, and all that this entailed, was done. One feels quite sure that the ratio will be an adequate one, so that the progressive methods described will be possible of achievement.

The history and development of nursing education in Teacher's College, Columbia University, is of great interest as it shows the importance and extreme usefulness of special training for the senior appointments in hospitals and it must turn out women highly qualified for the important positions of administrators of training schools for nurses, teachers in schools of nursing, public health appointments, etc. The history of nursing education is fully described and is of absorbing interest.

The article regarding development of nursing and schools of nursing on page 6 (from the Vanderbilt University Nursing School) should not be missed as it acknowledges many practical problems which arise in the training of nurses, and contains clarifying paragraphs such as 'a certain proportion of nursing schools have been created because hospital authorities thought they saw in them a good economic investment' or again 'It is quite obvious that these hospital authorities have been quite unaware of the social significance and social worth of nursing to the community' and again 'the function of the nurse has changed considerably during the past twenty-five years as a direct result of the advance made in the knowledge of science as it is applied to sickness and health—each year the nurse has been called upon to assume increasingly complex and responsible technical duties. She requires therefore an increasingly richer science background and a greater understanding of medicine which the nursing curriculum does not as yet provide'. Reference is also made to one of the basic principles laid down by Florence Nightingale that it is necessary for the nurse to be a woman of refinement and culture, because the art of nursing can never be practised by the mentally dull or by untutored individuals of no social graces. Information of a very useful kind is also given regarding 'nursing and the hospital' and the necessity for the inclusion of nursing in the hospital budget and its due importance. It deplores the fact that many hospitals treat the department of nursing as a non-revenue bearing unit, instead of showing in the hospital accounts the revenue derived from the nursing service which may run into thousands of dollars.

Other interesting articles from America and Canada follow and the 'Report of a Study made by the National Organization for Public Health Nursing' in New York is especially so and suggests the linking of practice with theory in a definite way, for example:—'..... the adapting of diets ordered in certain diseases to actual conditions under which the patient lives, and the relation of the patient's occupation to his treatment'.

The importance of the out-patient departments as units of experience is clearly shown as is also the observation home-visits.

The teaching of public health nursing in Toronto shows a very sincere effort to evolve the ideal training of the nurse for this particular branch of work.

China, one gathers, is attempting to train nurses in college, with visits to the hospital wards and departments, and one reads on page 136 'that the hospital has never depended for its care of patients upon the services of the student nurses'. The description of the training might be termed revolutionary as it appears to upset the strong tradition of the training of a hospital nurse in actual practical nursing which has hitherto been considered essential.

Denmark and Finland give interesting accounts of State Preliminary Training Schools, which fill a most important place and their example might be followed

with advantage in other countries. Much of the theory of nursing is taught in these schools so that when the student nurses enter the hospitals for training their attention can be largely concentrated on the actual nursing of the patients. The schools are state subsidized and the student nurses are drafted to the various hospitals for training on completion of this preliminary course.

In England many of the great hospitals have a preliminary training school for nurses attached, which has the advantage that the student nurse is taught in actual conjunction with the hospital and works for short periods daily in the wards of the hospital to which she belongs. One felt distinct disappointment on reading the article on 'Nursing Education in England' that so little description was given of the methods in daily use in the training of the nurse in actual practical nursing. It is such a feature of the training in English hospitals and a full description would have been of great value in a book of this type.

France is making great efforts to raise the standard of nursing and the work described is very interesting and tells of the same difficulties and uphill fight to establish nursing that so many countries have experienced. It tells also of the courage which has met and overcome these difficulties.

In 1903 no uniform was worn by the nurses and the strongest resentment was expressed at any suggestion of it. The example was set by the 'Directrice' allowing, as a great privilege, the new probationers to wear the same uniform as she herself wore, with the result that shortly all the staff were asking to be allowed to wear it. There was also no night nursing at all as it was considered improper for young nurses to nurse male patients at night. A system of night nursing was started with elderly women present to act as supervisors, until prejudice was overcome. From these beginnings great developments have arisen and the account of present-day methods of training are most instructive.

The account of the Siriraj Hospital, Bangkok, puts forward its problems and schemes for the training of nurses.

It is interesting to see the importance attached to hospital house-keeping in this article. Many of the problems which arise with regard to supplies and equipment were touched on and improvements recorded in the care of the soiled linen of the hospital by the erection of an electrically-run steam laundry. The linen supply and sewing room of this hospital are under the supervision of a nurse. A very practical point mentioned was the special course of instruction given to the coolie staff in general cleaning duties by a nurse instructor.

The publication contains much information of great value and is recommended for particular study in every province in India where nursing is so much in need of reorganization and assistance. Many of its suggestions and ideas set a great example and the whole volume will be a valuable guide to hospitals wishing to provide an adequate and progressive nursing service.

ABSTRACTED FROM THE REPORT ON THE ADMINISTRATION OF THE EXCISE DEPARTMENT IN THE PRESIDENCY OF BENGAL FOR THE YEAR 1931-32

THE excise administration is perhaps the one most concerned with the control of drugs of addiction in this country. While habitual use of the narcotics, stimulants or intoxicants is a necessary corollary to civilization and more active modes of life in any country, it must be admitted that moderate use of at least some of these substances is considered necessary if not altogether beneficial. The duty of the excise department of the Government is to see that the amount used does not exceed the safety limits, and the temptation is kept as far off as possible. The problem is being vigorously attacked in all its aspects in all civilized countries, but in India where probably the addiction problem is the

oldest and most widespread, it is yet to be seriously grappled with.

Calcutta is the largest city in India and on account of its commercial importance exacts a good deal of vigilance on the part of the excise, police and customs authorities. This is one of the main headquarters of the smugglers and it is evident from the summary of the prosecutions given in the report of the administration of the excise department in the Presidency of Bengal, 1931-32, that all the alertness, skill and tact of the department is needed to control this illicit traffic. During the year under report, 9,312 persons were prosecuted for offences against excise and opium laws as compared with 8,218 during 1930-31 and 1,033 ounces of cocaine were seized. The report shows that there is a reduction in the consumption of all excisable articles (though the revenue in some cases is more) in the year 1931-32 compared with the previous year and the Commissioner rightly points out this fall is due to nothing else than the general economic depression. The policy of maximum revenue with least consumption has had the desired effect in reducing the consumption, but this cannot go beyond certain limits, and these seem to have been reached. This only points to the necessity of starting scientific investigation of the problem, from medical, sociological, and economic aspects.

Another important aspect of the administration from the medical view-point is supervision of the supplies of rectified spirit used for manufacturing tinctures and medicines. Eight bonded laboratories in Calcutta and one at Konnagar continued to manufacture tinctures and medicinal preparations during the year under report. The rules prescribing strict adherence to B. P. standards and approved recipes continued to be strictly enforced, and there was no complaint regarding the quality of the products of the bonded laboratories. The working of the bonded laboratories was on the whole satisfactory and the medicinal preparations manufactured therein continued to be freely used both in Bengal and in the other provinces, replacing to a great extent the imported drugs from abroad.

R. N. C.

ABSTRACTED FROM THE ANNUAL PUBLIC HEALTH REPORT OF THE CENTRAL PROVINCES AND BERAR FOR THE CALENDAR YEAR 1931

DURING the year under report considerable activity has been shown in infant welfare work and that this is badly needed is shown by the infant mortality rate returns which are the highest for the province since the year 1921, and which from a table given in the report are shown to be by far the highest of any of the ten provinces for which figures are given. It is true that the birth rate is also higher in the Central Provinces and Berar than anywhere else but the infant mortality rate appears to be disproportionately greater.

There appear to have been no serious epidemics during the year but the total deaths from all causes show an increase of more than 25,000 over those of 1930; all the principal headings under which deaths are recorded showed an increase with the exception of cholera, smallpox and injuries.

ABSTRACTED FROM THE ANNUAL REPORT OF THE UNION MISSION TUBERCULOSIS SANATORIUM, AROGYAVARAM, NEAR MADANAPALLE, SOUTH INDIA, 1931-32

THIS interesting report is copiously illustrated and shows the sanatorium to be situated in attractive and spacious surroundings.

There are various types of accommodation in special wards for which payment from Rs. 50 to Rs. 100 per month is charged. In the general wards the small charge of Rs. 18 a month is made for those who can afford it, but this amount may be reduced at the discretion of the medical superintendent. Indigence, however,

is not a bar to admission as anyone with a certificate from a gazetted government officer may be admitted free.

This institution appears to be deserving of public support.

ABSTRACTED FROM THE ANNUAL REPORT OF THE KING GEORGE THANKSGIVING (ANTI-TUBERCULOSIS) FUND FOR THE YEAR 1932

This report gives an account of the activities in connection with the fund. There is an annual income of over Rs. 50,000 from invested funds and less than one-third is spent on administration.

The work of the organization is mainly propaganda and education of the public and under its auspices anti-tuberculosis sub-committees have been formed in many provinces and also in Mysore. Apart from running expenses nearly all the rest of the money expended during the year was disbursed as grants-in-aid to these various local sub-committees.

This fund with its steady income and wise expenditure should in time become a valuable force in combating tuberculosis in India.

ABSTRACTED FROM THE REPORT OF THE THIRTEENTH EPIDEMIC OF PLAGUE IN THE CITY OF HYDERABAD AND ITS SUBURBS

The spread of infection in this epidemic was almost entirely by human agency, either (1) by removal of a case of plague, (2) by carrying infected clothing, (3) by entertaining relatives or friends from infected areas, (4) by visiting the sick. In all these cases infected fleas are carried in the bedding or clothing of either the sick or the healthy to the non-infected house. These infected fleas carry the disease to the rats in the new house or to the human inmates, but as a rule the fleas first infect the rats and only bite the human beings after the rats are dead. A plague-stricken rat loses its natural defence against fleas and sometimes swarms with them—enormous numbers of fleas in this way become infected and the people in the house have small chance of escaping infection. In some cases the fleas in the new house may be infected directly by the imported case of plague. It is interesting to note that when hundreds of plague cases are admitted into the isolation hospital the complete disinfection of the clothing and bedding has been sufficient to prevent a single case of infection among the hospital staff.

Direct infection by visiting the sick is likely to occur when the visit takes place at night or in dark ill-ventilated rooms. Fleas are always inactive in bright daylight.

Once the infection has been brought by human agency to a new locality, its spread from house to house in that particular area is by rats. The theory that rats move far from their burrows or migrate from fear of an epizootic is not true of the house rat in India. In and from Nurkhan Bazaar infection only spread in definite proportion to human migration. Sultanshah which is only three to four furlongs away did not show signs of infection for at least three months from the outbreak of the epidemic. The spread of infection was arrested in nine localities and though sporadic imported cases occurred in these areas later on, there was sufficient interval to establish the claim that infection had been prevented. It is interesting to note that the number of infections in new localities of the town amounted to 207: in none of these did the disease spread to a great extent. It is felt justifiable to claim that this large number of isolated infections would normally have created, first of all a very wide infection of rats, and secondly a very severe epidemic of human plague; no part of the city or Chaderghat escaped invasion by the sick and their relatives from the infected area. The area of the town of Hyderabad is 35 square miles, and including the frontier villages it

is roughly 50 square miles. The actual deaths from plague average 20 per square mile; and this includes those definitely imported from other towns. The rapid arrest of all these isolated outbreaks was possible only because a very large proportion of rats had been destroyed. Another deduction which seems justified is that all the spread was due to human agency.

X. cheopis (the dangerous flea) is the most prevalent flea in Hyderabad. The variety known as *X. astia* is found only in certain areas, and comprises 6 per cent of the fleas in Hyderabad. *Astia* is found in a far higher proportion in the Madras Presidency which consequently is usually free from plague. Hyderabad is a city, which contains an astonishing population of rats and provides all the conditions favourable for their rapid breeding. Rats breed freely in the interstices of roof tiles and the 'kutchra' walls without foundation. Most of such walls and roofs are found riddled with rat-holes. As mentioned in the last report the circumstances are so favourable for breeding of rats that it will be impossible to keep the rat population under control without persistent and continuous destruction for years to come. While this destruction is going on, it is absolutely necessary to continue the work of the City Improvement Board in providing large numbers of good type of rat-proof houses and cleaning slum areas. Rat-proof gunjes and markets are to be constructed and special attention will also be necessary for hundreds of retail grain shops.

Food is always present in unlimited supply for these pests and the public require education in this matter. In every middle- and upper-class house there are godowns for storing grain all accessible to rats. Among the poorer classes remnants of food are not thrown away. These conditions provide food for rats in unlimited supply.

ABSTRACTED FROM THE REPORT ON THE HEALTH OF THE ARMY FOR THE YEAR 1931. VOLUME LXVII. LONDON

The following abstracts have all been taken from that portion of the report dealing with the army in India:—

Sand-fly fever.—In India as a whole the variation in the incidence of sand-fly fever shows little change over a series of years; but when individual stations or small areas are considered, very remarkable differences are seen, and with the exception of the effect of the presence or absence of 'salted' individuals, knowledge of the causes of these variations is very slight. Thus the ratio per 1,000 in Landi Kotal increased from 227.3 to 394.5 per 1,000, ascribed, probably quite correctly, to the presence of an 'unsalted' British infantry unit, but, in spite of this local increase, the incidence in the whole Northern Command fell from 123.6 to 72.1 per 1,000, a decrease in which all the plains stations shared. On the other hand, there was an increase of nearly 100 per cent in the plains stations of Lucknow and Meerut Districts.

In India, sand-fly fever is a disease of the comparatively hot and arid areas of the North-West Frontier and Northern Punjab, and in the plains the disease shows a tendency to occur in two waves, the first in April/May and the second in July/August. The second wave may be due to the return of susceptible individuals from the hills, but it is possible that climatic conditions are a determining factor. A study of the monthly figures of incidence gave no correlation with either rainfall or mean relative humidity, but a mean 8.0 a.m. temperature of over 70°F. and under 90°F. was associated with an increased incidence of the disease. Monthly figures, however, are too wide for the study of a disease with such a short incubation period and of such short duration. The question is further complicated by the admitted difficulty of diagnosis, particularly of cases occurring at the beginning or end of the epidemic season, which are very apt to be confused with influenza or malaria.

No really effective methods of prevention have been devised. Repellants such as P.C. oil are of limited value owing to their evanescent effect, while sand-fly nets are much too airless for use in a tropical climate. Spraying with insecticides will reduce the incidence of the disease, especially in small barrack rooms whose occupants have no night duties to perform. This, however, is an expensive measure and not applicable under field conditions.

Enteric fevers.—Of the 493 cases occurring among British and Indian troops, 254, or just over half, were diagnosed by the isolation of the specific organism, the remainder being classified as enteric group.

Blood culture remains the most certain method of diagnosis, although it missed 1 in 5 cases. Of the 48 cases which gave negative results, 95 blood cultures were performed; 4 in 3 cases, 3 in 9 cases, 2 in 20 cases, and 1 in 16 cases. In all but two cases the first culture was taken before the seventh day of the disease. Of the 195 positive cases, 153 were diagnosed on the first culture, 36 on the second, 5 on the fourth, and 1 on the fifth.

The results of faeces culture, as has been previously pointed out, do not represent the full possibilities of this method of diagnosis, for cases which have positive blood cultures in the early stages of the disease are considered to be diagnosed and have no faeces examinations carried out until convalescence. Even so, the results are disappointing.

A point worthy of note is that occasionally the organism is discovered in the stools on one or two occasions long after clinical convalescence has been established. This occurred in no fewer than 9 of the cases, i.e., 3.7 per cent. It is possible that this may be due to the shedding of material from healing ulcers, although no microscopic evidence of this has been noted.

The results of urine culture, like those of faeces culture, are not entirely representative. In this case, however, there are no difficulties of isolation to contend with, and it seems fairly certain that only a small proportion of cases in India excrete enterica organisms in their urine.

Dysentery.—There was a considerable increase in the number of dysentery admissions for the year, more than can be accounted for by the drop in the figures for diarrhoea and colitis. While this may be in part due to the fact that the troops are becoming more alive to the necessity of reporting sick whenever symptoms of diarrhoea manifest themselves, there is no doubt that it is also in part a true increase.

The figure for bacillary dysentery is almost identical with that of 1930. Protozoal dysentery has fallen by 2.7 per cent, and there has been a corresponding rise in clinical dysentery.

Treatment of dysentery has been along the same lines as in previous years. Polyvalent high potency (double strength) anti-dysenteric serum 'Hoechst' has been tried and very favourably reported on, and arrangements have been made to maintain a stock of this serum.

On the whole the cases have been of a mild type and have responded readily to treatment. Among the 1,593 cases occurring among British troops, one death occurred in a case diagnosed clinical dysentery.

Malaria.—The number of chronic relapsing cases sent to the Malaria Treatment Centre, Kasauli, has been declining of late years, and in 1931 only 126 cases arrived, compared with 241 in 1930. This marked falling off in numbers has been ascribed to the more general use of plasmochin, which is now included in the official list of drugs.

The main investigation both in the treatment centre and in the large hospitals has been directed towards determining the minimum effective dose of plasmochin. It is now accepted that 0.03 gramme of plasmochin plus 20 grains of quinine daily for twenty-one days will reduce the relapse rate to the neighbourhood of 5 per cent. In Poona 325 cases were treated with

0.03 gramme for ten days, followed by 0.02 gramme for eleven days, plus 20 grains of quinine daily. The relapse rate was only 2.8 per cent. At Kasauli two new courses of treatment were tried, viz:—

Plasmochin 0.01 gramme plus 20 grains quinine daily for twenty-one days—10 cases, and plasmochin 0.03 gramme plus 20 grains quinine for fourteen days—9 cases.

The numbers are very few, but so far no relapses have occurred after an average observation period of ten weeks.

Short courses of six- and ten-day treatments were tried in Quetta, but the results were not so favourable. Various observers have noted that retention in hospital for ten days has a beneficial effect in preventing relapses.

During the year a quantity of the new synthetic preparation, atebrin, was obtained. The producers claim that this drug acts equally promptly on the schizonts of both *P. vivax* and *P. falciparum* and cures the attack in five to seven days with 0.1 gramme three times a day. The drug apparently accumulates and continues to be excreted for varying periods up to twenty days after cessation of treatment. So far very few cases have been treated, but the results to date indicate that atebrin will cure the attack. If this drug proves effective in preventing relapses, then a combination of atebrin for five to seven days, with a short course of plasmochin during convalescence, holds out the promise of a cure, not merely of the individual attack, but of the infection. This would lead to the eradication of gametocyte carriers, and such a cure would be of inestimable benefit to the army.

On the result of James's experiments in London, it was decided to try plasmochin prophylactically during the operations in Burma. The earlier trials were promising, but the final results were not so satisfactory. It is considered that the favourable results in the early stages were due to the curative action of the drug rather than to any definite prophylactic effect.

ABSTRACTED FROM THE NINETEENTH ANNUAL REPORT FOR THE OPHTHALMIC SECTION OF THE DEPARTMENT OF PUBLIC HEALTH: MINISTRY OF THE INTERIOR, EGYPT, 1931

This report opens with a series of thirty-eight of the forty-nine photographs which have been opened in Egypt between the years 1904 and 1932. Some of these hospitals are large imposing buildings and a glance at the photographs gives perhaps a better idea of the extent of ophthalmic work in Egypt than many pages of a written report would do.

The amount of work done is shown in the following table:—

	1930	1931	Increase in 1931
			Per cent
New patients ..	526,406	634,088	20
In-patients ..	20,136	22,188	10
Operations ..	209,662	220,823	5
Out-patients attendances.	4,350,062	5,023,175	15

ABSTRACTED FROM THE REPORT OF THE HAFKINE INSTITUTE FOR THE YEAR 1931. BOMBAY

The institute continued to function during the year as (a) the centre for manufacture of plague vaccine for the whole of India, (b) the provincial bacteriological laboratory for the Bombay Presidency, (c) the centre for manufacture of antirabic vaccine for Bombay

Presidency and adjoining areas, and treatment centre for Bombay city, and, in addition, carried out research work on plague and other subjects as in former years, largely with the assistance of the Indian Research Fund Association.

Plague work.—The manufacture of the vaccine has, as in former years, constituted the main activity of the institute. The demands for vaccine continue to be high in proportion to the incidence of plague mortality, and the slight rise in plague during the year over the number of cases occurring during 1930 was reflected in an increase in issues. It has been shown in previous reports that a regular increase in demand in relation to cases occurring has continued in successive years, and the proportion of issues in the present year has been 31 doses of vaccine for each plague death registered. During recent years the institution of a fresh experimental investigation into the vaccine and its properties, and into the effect of each procedure employed in preparation has resulted in undoubted improvements. Experimental evidence has shown an increase in its immunizing value as the result of the use of revised methods. Such statistics as are available as to the protective value of vaccine prepared in recent years as compared with older results also suggests a marked increase in potency.

The methods introduced by Dr. Gore for the preparation of pure strains of *B. pestis* from passage animals for seed purposes have been found to be fully effective. The differential methods for determination of purity which are now used have ensured that the losses of vaccine under preparation which formerly occurred due to the use of impure seed could be completely avoided.

The relationship of virulence to potency and toxicity to potency have been studied and also the effect of the period of incubation, temperature of incubation, reaction and composition of medium on the immunizing value of the vaccine. The question of a technique for biological standardization of the vaccine has been the subject of further study. A prolonged series of experiments with different brews of vaccine has given consistent results, but at intervals difficulties have been experienced due to changes in virulence of the passage strain of *B. pestis*. It is hoped that when this difficulty can be overcome the method of testing will afford a reliable means of ascertaining the value of successive brews and of comparing the potency of vaccines prepared by variations in technique by entirely different methods. The technique has been applied to the comparison of the relative value of Haffkine's vaccine to agar-grown and 'derived' vaccines prepared by other laboratories. The results of some of these tests are given in the research section of this report and only one vaccine has been found to compare with the Haffkine vaccine, this being a vaccine of high bacterial content and toxicity. Chemical studies of the changes occurring in the vaccine during the period of incubation have been carried out with the object of ascertaining the probable immunizing fraction.

Many of the sera prepared have been of high potency as tested on experimental animals and a trial on a short series of human cases has given very promising results.

The pharmacological unit.—The principal investigation carried out during the year was in connection with scorpion stings. The properties of the scorpion venom were very fully studied. The toxicity of the venom of various species was determined in relation to body weight and the conclusion arrived at that a scorpion sting could in no case be fatal to a normal human being. The various traditional Indian plant remedies for scorpion bite were investigated and found to be without value.

The biochemical unit.—An extensive investigation was undertaken into the normal standards of chemical constituents of the blood of adult Indians in order to establish a basis for a future investigation into the changes occurring in the blood in kidney and other diseases in persons whose dietary and, in particular,

whose protein intake differs widely from that used in western countries for which standards have been established.

The antirabic department.—The number of cases of dog-bite receiving prophylactic treatment has, as in former years, shown a progressive increase. The total dealt with at the institute rose to 1,061 with a mortality of 0.28 per cent which compares very favourably with that of other institutes in India. In addition to these cases 5,998 were treated at out-centres. The results for the last two years since the introduction of the use of the Paris strain of fixed virus and graded courses of treatment according to the assessment of risk have been the best recorded. A corresponding improvement has not taken place in regard to cases treated at out-centres. The majority of the institute cases are from Bombay city itself and the early stage at which cases attend for treatment and the thorough immediate disinfection measures adopted may be responsible in some degree for the better results obtained. The first case of a 'paralytic accident' amongst those treated with vaccine prepared at this institute was recorded during this year. The case fortunately ended in complete recovery.

ABSTRACTED FROM THE DIRECTOR'S REPORT OF THE LEAGUE OF NATIONS HEALTH ORGANIZATION ON THE WORK OF THE EASTERN BUREAU FOR THE YEAR 1932

ADVISORY COUNCIL

The year under review was the only one since the Bureau was established in which no meeting of the Advisory Council took place.

The greater part of the report consists of detailed accounts of health conditions in the chief ports of the East during the year under review and is therefore only of historical interest. The organization of the Bureau whereby all countries in the Eastern hemisphere are advised every week of the state of chief epidemic diseases everywhere in the area is fully described and on account of its importance it has been fully abstracted below.

EPIDEMIOLOGICAL INTELLIGENCE

This service constitutes the main function of the Bureau. It has been steadily built up in the eight years that have elapsed since the Bureau commenced to function and consists of three divisions for the reception, collation, and distribution of information.

Reception.—The reception service covers the whole of the Eastern arena, extending on the West as far North as Alexandria and Syria; on the South-West to the Union of South Africa; on the North-East to Vladivostok; on the South-East to Australia and New Zealand, and as far into the Pacific as the Hawaiian Islands. From all the Health Administrations of this extensive area communications are received regularly by cable or by post.

Cables.—The cable service comprises an emergency one, under which immediate information is forwarded concerning the first appearance of plague, cholera, small-pox or other communicable disease in epidemic form in the ports, and a regular one comprising a routine weekly cable giving the position in regard to these diseases each week in the ports and provinces.

The outstanding feature under this section for the year has been the taking over by the National Quarantine Service of China, on and from 6th April, of the quarantine services of Chinwangtao, Tientsin, Tangku and Taku. From the headquarters of this service at Shanghai returns are now regularly received concerning the existence of infectious disease in Hankow, Nanking, Shanghai, Amoy, Swatow, Canton, Tientsin, Tangku and Taku, Antung, Newchwang and Harbin. Unfortunately there is not the same degree of accuracy in the returns from each of these ports, and particularly does this apply to Swatow, where the quarantine administration is dependent on the Health Department

for information. This lack of accuracy is all the more to be regretted because unofficial reports arrive at the Bureau from time to time which suggest that the health of the port may be less satisfactory than official communications indicate. Swatow has a considerable trade with ports of other countries, and owing to the uncertainty which exists, quarantine measures which may or may not be in conformity with actual requirements are liable to be taken by these ports.

From the Head Office of the Netherlands East Indies Public Health Service, Batavia, information has been received that the number of N.E.I. ports from which communications are received, and in regard to which returns are sent to the Bureau, is now twenty-six (26).

Number of ports.—The number of ports in regard to which information is now received by cable amounts to one hundred and sixty-three (163).

Postal.—By post supplementary information is received weekly confirming the routine cable, giving further information in regard to the state of communicable diseases in the provinces and districts, as well as information as to meteorological conditions, birth and death rates, mortality rates from certain diseases, particulars regarding rat destruction operations and measures taken against infected ports. In addition to weekly information, four-weekly postal returns are received from a number of Health Administrations, while annual reports from the greater number of these also come to hand.

CO-ORDINATION OF INFORMATION

The information received in the routine cables refers to the condition which existed during the preceding week ending at midnight each Saturday. This information begins to arrive at the Bureau on Monday, but it is not until Wednesday morning that the bulk of the returns are to hand. In the case of certain countries, particularly British India, owing to the number of provinces to which the returns relate and the consequent delay in receiving information at Delhi, it is not until Thursday morning that all returns are finally received. During these four days the information is sorted out and arranged for distribution. This comprises decoding of separate cables and combining their contents into comprehensive general cables and coding them for distribution. The material contained in the weekly postal returns is at the same time into the form in which it can be used in the published by the Bureau.

DISTRIBUTION SERVICE

The methods of distribution are wireless transmission, telegraphic communication and postal circulation of a The information for the week is transmitted by cable each Thursday morning to Saigon where, through the courtesy of the Government, it is emitted from the powerful wireless station each Friday morning in code. This message is picked up either directly or indirectly throughout the whole of the area from which information is received. The East coast of Africa receives the message indirectly through the intermediary of the station at Tananarive, which picks it up and re-transmits it each Saturday morning. The Saigon message is also picked up by the Malabar Station, which transmits it in code each Saturday morning both on long and short wave. In addition, certain Administrations summarize the decoded message and re-transmit it in clear in an abbreviated form. This is done from Hongkong, Karachi, Madras, Sandakan, Shanghai and Tokio weekly, and from Malabar daily.

The most noticeable advance in connection with the wireless transmission would be the addition of a clear message from Saigon as well as the code message. Through the courtesy of the Government of Indo-China it appears likely that this will be possible in the very near future. The proposal is that the message should be transmitted in code followed by transmission in clear in the English language on short wave. The translation from code to clear message will be carried out by arrangement with the Inspector-General of Medical and

Sanitary Services at Hanoi by the local Director of Health at Saigon. This will meet the request of many Eastern countries for transmission in clear instead of in code, and at the same time allow those Administrations which still desire a code message to receive it.

Quarantine notifications.—In addition to notifying the incidence of disease, one feature in the wireless messages is the inclusion of information concerning the measures taken by particular ports to protect themselves against infection which exists in other ports. Each week these notifications are brought up to date, and quarantine procedure can now be based on an actual knowledge of the diseases which have to be guarded against.

Transmission in clear.—To meet the requirements of ships' masters who desire to know the prevalence of major communicable diseases in the ports with which they are trading, a message in clear is transmitted daily, by the courtesy of N.E.I. Government, from Malabar. That this message fulfils a need is shown by the fact that it is regularly picked up by steamships of different flags. A proposal was put before the recent Conference at Madrid which had under consideration the revision of the International Radio-telegraphic Convention of Washington, 1927, that the Bureau's messages should be classed for the East as 'Special Services' under the Convention. This, however, was not approved, and in consequence the full value of the service cannot at present be realized.

During the year only one failure to pick up the Saigon broadcast has been reported, and this was by British India. The reception of this message, which was transmitted on the 23rd December, was interfered with by atmospherics, but this difficulty was overcome by picking up the clear broadcast from Malabar.

TELEGRAPHIC COMMUNICATION

Emergency cables.—Cables notifying the appearance of 'first cases' are immediately despatched to Geneva and from there to Paris. In addition, this information is immediately re-transmitted by cable to all ports having trade relations with those in which these 'first cases' have appeared. This gives the health authority warning of the potential danger, and enables steps to be taken in advance to meet it.

Routine cables.—Twice a week, namely, on Wednesdays and Thursdays, cables are forwarded to Geneva, and from Geneva to the Office International, Paris, which contain a summary of all the information received for the previous week. The despatch of these cables complies not only with the desire of Geneva for information for distribution, but also with the obligations which the Bureau has undertaken as an agent for the Office International, Paris. These cables arrive in Europe in time for their contents to be included in the Weekly Record published at Geneva by the Health Organization.

Cablegrams are still required for despatch of information to certain ports which are unable to pick up wireless messages, or are only able to pick up a re-transmitted abbreviated summary of These ports are Vladivostok, Canton, Aden and Seychelles.

Infected ships.—Cabled information that a ship infected by one or other of these diseases is on its way to a particular port is of great value, both to the Port Health Authority and the agents of the ship. Every endeavour is made to obtain information at the earliest possible moment regarding the next port of call of any infected ship, as well as the nature and extent of the infection and the measures which have been taken to control it. This information is transmitted to the next port of call with the result that duplication of precautionary measures need not occur, and the Port Health Officer is enabled to apply only such measures as are necessary to protect his population.

Weekly fasciculus.—In order to supplement the information transmitted via wireless and cables, a Fasciculus is published each week which confirms the news sent by the other methods and includes a great

deal of additional information relating to the state of countries and provinces as regards the existence of other infectious diseases. This Fasciculus also supplies information regarding the movement of population between various ports, both regular movement and movement at times of pilgrimages. The notification of quarantine measures applied against various ports is brought up to date and a list is given showing those ports which have been infected with plague, cholera and smallpox during the preceding 12 months, together with the date of the last infection.

The Fasciculus is now distributed directly from the Bureau to a number of Health Officers in the Federated Malay States who previously received their copies through the intermediary of the headquarters of their Department in Kuala Lumpur. Additional copies of the Fasciculus are this year being required for distribution to a greater number of institutions and health workers in Japan who have requested to be put on the mailing list, and to Medical Officers of estates in Malaya.

By the use of these three methods it is possible to ensure that every public health administration in the East knows within a few hours of the occurrence of any fresh outbreak of plague, cholera and smallpox in ports with which it has direct trade communications. It is possible to ensure further that every health administration knows the state of health of each one of the 163 ports from which information is received, up to the previous Saturday night, and at a later period that each health administration is possessed of detailed information regarding the state of health of countries in the East, as well as the state of health of the ports of such countries.

MALARIA COURSES

Arising out of Prof. Ciucea's visit, when tentative discussions took place regarding the establishment of international malaria courses in the East, arrangements were come to with the Medical School at Singapore whereby the latter was to carry out the technical work, if it were decided by the League to establish these courses at Singapore. The proposal has now been approved, and preliminary arrangements are in hand for the first of these courses to commence on 30th April, 1934. It is proposed that the League should bear the expense of five fellowships, which will be offered to administrations which are prepared to send an additional member to the course at their own expense. It is hoped that there will also be a number of entries from Eastern Governments and from practising physicians.

The League proposes that the theoretical work should be carried out at Singapore and the practical work in several Eastern countries, the arrangement being that members of the course should have the opportunity to study field work in a country other than the one in which they are themselves working. The League also proposes to bring two experts each year from overseas to assist in the course.

The estimated cost per annum, namely, 38,000 Swiss francs, will be borne by the Budget of the Health Organization.

ABSTRACTED FROM THE REPORT OF THE BOMBAY SOCIAL HYGIENE COUNCIL FROM JULY 1931 TO DECEMBER 1932

THIS report covers the half-year ending December 1932 during which period the Council entered in its sixth year of existence. But the formation of this council and its affiliation with the British Social Hygiene Council in 1926 does not mark the beginning of organized effort in Bombay to deal with venereal disease, because the present body arose out of the League for combating Venereal Disease which had been in existence since 1917.

SEAMEN'S WELFARE IN PORTS

The prevalence of venereal diseases in the mercantile marine is considerable. The continued change of venue

of its members and the temptations for misconduct existing in most seaport towns are factors that loom large in the life of a seaman. Seamen's welfare in ports is therefore at once an international problem which can only be solved by the maintenance of treatment facilities for those who have been infected and the provision of such measures as will tend to prevent cases of infection at the seaport. The importance of both these aspects is emphasized by the fact that in 1924 an International Convention was instrumentalized through the Belgian Government under the title of Belgian Agreement by which the contracting governments 'agreed to create and maintain in each of their principal ports, whether on river or sea, venereological services open to all merchants, seamen or boatmen without distinction of nationality'. Under this scheme a seafarer obtains treatment at every port of call. Any person treated at any of these international centres receives a *continuation case book* in which the medical officers of the various clinics visited, enter details of diagnosis and treatment and the case is thus followed up.

Over 20 nations have adhered to the terms of the Belgian Agreement and have taken definite action on it. But the Government of India, though approving of the principle underlying the scheme, has not accepted it, and India therefore remains an international offender..... However, within the British Empire, while Great Britain, Australia, Canada, the Irish Free State and New Zealand are signatories to the Agreement, many of the colonies, mandated territories and protectorates provide good facilities for the diagnosis and treatment of venereal diseases in seamen though they have not accepted the Agreement and our position in Bombay is evidently analogous to that of the latter countries.

The port of Bombay is one of the largest in India. It is visited by European, American and Asiatic ships. The total number of ships visiting the port each year is 3,951 and the average crew about 60 per ship, so that roughly 240,000 members of the mercantile marine visit the harbour each year. There is besides a considerable number of native craft estimated at about 10,000.

It is imperative therefore that we should organize a voluntary anti-venereal service for the seamen. It would lessen the infection among our floating population, while it would lessen the risk of their infecting the civil population. Above all it would tend towards the fulfilment of a duty to the world nations who have a right to expect us to treat their men as they treat ours. The Bombay Social Hygiene Council has therefore striven to promote those measures which fall in with the spirit of the Belgian Agreement and which will make Bombay a voluntary contributor to the international scheme. During the year under review we have met with a certain amount of success in our efforts.

GOVERNMENT V. D. CLINICS

Facilities exist and more are being brought into existence in government and municipal clinics for the treatment of seamen. As an additional measure of more handy relief we suggested to the Government of India the establishment of a centre in the vicinity of the docks. In reply they have informed us that since the St. George's and the Gokuldas' Hospitals are not very far away from the harbour a scheme is under consideration by the local government for providing special arrangements at these hospitals for the treatment of seamen suffering from venereal diseases. It is gratifying to note that government are moving in the matter.

PORT TRUST DISPENSARY

In accordance with a resolution passed at the general meeting of the council held in August 1929, the Chairman of the Bombay Port Trust was requested to consider the necessity of including modern diagnosis and treatment of venereal diseases in the scheme of a

new dispensary that the trust was contemplating. We received a reply that the matter was receiving attention but as a result of further correspondence we have now been informed that the scheme has been postponed for financial reasons and that the Board is of opinion that when it comes to fruition treatment of V. D. cases should be restricted to the employees of the trust for whose benefit the dispensary existed.

We have no grounds for criticizing the decision of the board. But till such time as a Port Sanitary Authority comes into existence, we hope the Bombay Port Trust will re-consider the matter and contribute their quota to the solution of the problem by throwing open the port trust dispensary for the disinfection and treatment of infected seamen.

The seafarer is an agent in the prosperity of the port. Under the Consolidated Act, the Port Trust gives grants to local institutions which promote the welfare of seamen. We suggest that the claim we put forward is urgent and necessitous and we hope the Port Trust will make the necessary provision.

INFORMATION TO SEAMEN

On the suggestion of the Port Officer, Bombay, and at the request of government we undertook the publication of a pamphlet in four languages, English, Gujarati, Urdu and Konkani for the guidance of seamen, pointing out the dangers of venereal diseases and giving particulars of the medical facilities for diagnosis and treatment at the Port of Bombay. These pamphlets were very kindly printed at the expense of government and are now being distributed to seamen by the Port Officer and Shipping Master of the Port of Bombay and by the Secretary, National Seamen of India Institute.

CONTINUATION CARDS

The Surgeon-General with the Government of Bombay and the Executive Health Officer for the city have kindly agreed to provide for *Continuation Case Books* according to the international pattern in the case of seamen patients applying for treatment at the government and municipal clinics. This is a measure which will enable these patients to obtain treatment in continuity at all ports of call as enacted by the Belgian Agreement.

SOLICITATION AT THE DOCKS

The attention of the Government of Bombay was drawn to Question No. 6 of Report III of 1931 of the International Labour Conference on 'Promotion of Seamen's Welfare in Ports' and the council wrote to inquire whether government was of opinion that soliciting and enticing of seamen in the harbour area should be prohibited and if so what steps government proposed to take in the matter. We received a reply to say that the Governor in Council was of opinion that it was desirable to prohibit the soliciting and enticing of seamen in the harbour area but government's information was that there was no actual soliciting in the docks in Bombay. In consultation with the Bombay Vigilance Association it was pointed out to government that while admitting that there may be no obvious solicitation in the docks the fact that women could board certain ships when they arrive in the docks tends to produce the same results as open solicitation. Also apart from the women themselves soliciting there were the victoria drivers who were potential pimps. We have now received a reply from government to say that it is reported that the masters of ships who allow women on board are masters of vessels which are foreign, i.e., neither British nor Indian; that it has to be remembered that many foreigners take a different view of this question and allow women on board their ships not necessarily because they are prostitutes but oftener than not because they are of the same nationality as the ship and possibly because they have friends on board. Under the circumstances it could not be proved that these women go on board on every occasion with the express object of soliciting and in any case the responsibility for preventing access of persons

of this description to a ship rested with the master and not with the police as it was within the power of the former to issue orders for undesirable visitors to be refused admission on board. In order to exercise some sort of check it was necessary to secure the co-operation of the masters of the ships and the government proposed to address the Shipping Master, Bombay, in the matter and to ask for his co-operation. In connection with other solicitation government intimated that their information was that the number of professional pimps who can obtain access to the dock area in Bombay without being detected by the police was negligible and agreed that the licensed drivers of public vehicles were a potential source of pimps.

We are awaiting further communication in this matter regarding the action of the Shipping Master.

RECREATIONAL FACILITIES

The steps taken to reduce the spread of diseases from country to country are, besides the provision of medical facilities, an increase of recreational facilities, shore sleeping accommodation and attention to the social conditions of the ports. Experience gained in the various armies and navies has led to the recognition of the fact that direct relationship exists between recreational facilities and the incidence of venereal diseases. Where counter-attractions exist there is less promiscuity and, consequently, less venereal disease.

The Prince of Wales Seamen's Institute for Europeans is an excellent institution run in connection with the Missions to Seamen and erected on land provided by the port trust. It has been in existence for some years. We welcome the Indian Seamen's Home which was recently constructed also on land provided by the port trust as a memorial to Indian seamen who lost their lives in the war. It is a splendid building designed to accommodate and recreate lascar seamen, and we welcome it all the more because although the need of it had been recognized for many years and a considerable proportion of the required funds was available, no constructive action was taken until the delegates of the British Social Hygiene Council visited Bombay in 1926 and took the matter up with government.

We realize that it is necessary that government should allocate a special playground to the mercantile marine and contemplate reiterating the request made to government by the delegates of the British Social Hygiene Council, that such a provision be made when the Back Bay Reclamation Scheme is completed.

On account of lack of space we regret we are unable to abstract from this report more fully but in addition to the work outlined above the council is engaged in educational propaganda including an exhibition at the national baby and health week association held at different mulls every week, writing articles for insertion in popular vernacular magazines, and courses of lectures to social workers. Owing to their efforts it is hoped that the council will soon have prophylaxis centres at the public hospitals and information regarding these posted up in the public urinals.

It is impossible even to mention all of the many activities of this body of voluntary workers, but perusal of the report shows that they are fully alive to the danger of venereal disease in all its aspects and they are attacking its many problems in the most enlightened manner.

Not the least remarkable fact in this campaign is that the total cost of the work for the year 1932 is only fifty-six rupees fifteen annas which shows this movement is truly honorary, and Bombay is fortunate in the possession of a body of such energetic and public-spirited workers.

ABSTRACTED FROM THE EIGHTH ANNUAL REPORT OF THE PASTEUR INSTITUTE, CALCUTTA, 1931

The total number of patients who attended the institute for treatment and advice during the year was

10,426 as compared with 9,094 during the previous year. This is the highest figure yet obtained. Of this number, 7,761 were given a full course of treatment, 1,737 were given advice only as no treatment was considered necessary in their cases, and 823 patients voluntarily abandoned treatment (absconders). The number fully treated exceeds the previous year's corresponding figure by 803 and the number of absconders by 140. The figure of absconders is very high, there is no control over these cases as most of them are non-indigent and come at their own expense for treatment.

Treatment.—The vaccine used for immunization is prepared by Semple's method from sheep's brain with the Paris Fixed Virus. The strength of the emulsion used is 1 per cent and the dose is—

Licks—5 c.c. daily for 7 days.

Bites—5 c.c. daily for 14 days for all classes of cases.

Results of treatment.—The statistical results are based on the health returns of patients 6 months after completion of treatment. The total percentage of these returns for all cases during the year is 67.9 per cent. Great difficulty has been experienced in tracing the patients at the end of the 6 months' period and numerous replies from district and despatching officers have stated that the patient had left the village and his present whereabouts are not known.

There were 57 deaths from hydrophobia during the year. Of these 14 arrived at the institute after the disease had developed and are excluded from the deaths. Of the remaining 43 deaths, 8 developed the disease during treatment and 7 within 15 days of completing treatment and are regarded as 'Non-failures'. The remaining 28 cases developed the disease after 15 days of completion of treatment and are regarded as 'Failures', giving a total death rate of 0.55 per cent and a failure rate of 0.36 per cent for the year.

There were no deaths among the 254 European cases treated during the year.

Decentralization of treatment.—It has not been possible to issue vaccine to treatment centres owing to the limited accommodation available for the work of this institute. The bottling of vaccine in ampules, which is the only safe method of issuing vaccine to out-stations and treatment centres, cannot be undertaken at present for want of proper accommodation. A scheme for the reorganization of the institute and the provision of more accommodation so as to start a bottling section has been submitted to government and should it be accepted, the bottling section will be opened and the vaccine issued to treatment centres. This will relieve the present congestion which exists besides greatly reducing the total cost of the upkeep of the institute.

Correspondence

MODI'S MEDICAL JURISPRUDENCE

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—With reference to the review of his book which appears in the June number of the *Gazette*, Dr. Modi has made the following comments:—

'The tables re. the ages at which the epiphyyses of long bones unite, etc., were adopted by the author in consultation with the Professor of Anatomy of the King George's Medical College, Lucknow, and the Radiologist, King George's Hospital, Lucknow, whose investigations do not concur with those of Dr. Galstaun. They were aware of his article in the *Indian Medical Gazette*.'

Re. the remarks of the reviewer about the treatment of arsenic poisoning by sodium thiosulphate his attention is invited to the following paragraph on p. 681 of the book under review:

'George W. Lawson, W. P. Jackson and George S. Cattanaeh recommend the intravenous injection of 7½ grains of sodium thiosulphate in 10 per cent solution. They tried it in 28 cases of poisoning by arsenic after the stomach was washed out with warm water. Of these 15 recovered and 13 died from 6 hours to 13 days.'

Yours, etc.,

BUTTERWORTH & CO. (INDIA), LTD.

CALCUTTA,
4th July, 1933.

VACCINATION AGAINST SMALLPOX

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—In the letter of 'C. L. B.', Bombay, published on page 359 of your issue of June 1933 under the heading 'Vaccination against Smallpox', it is stated by him:—'I object to the circular drill seemingly approved in the last paragraph of Colonel Stewart's note' and further says:—'In highly skilled hands the drill may possibly be successful, but I submit that it can never be as good as a cutting edge or point'. I do not agree with this view, and would offer below a few remarks on the subject.

There is no doubt that the vaccination operation is a trivial one, but all the same it requires a certain amount of skill and practical experience to have it done as it should be to obtain satisfactory results. It is seen that a considerable number of failures or cases reported as 'unsuccessful' or even 'insusceptible' in the hands of one vaccinator are found to show quite a 'successful take' in the hands of another vaccinator, this, of course, irrespective of the quality or potency of the lymph used. The technique of this little operation varies considerably, not only throughout India but also throughout the world. Each country and even each individual seem to adopt his own method considering that to be the best one. Linear incisions with an ordinary scalpel or other cutting-edge vaccinating lancet are the ones generally adopted in Europe. Dr. Force in America used his drill method, which consists in applying vaccine lymph to a two-millimetre circle of derma exposed by removing the epidermis by means of the rotatory motion of a small drill held perpendicularly to the tightly-drawn skin. On the other hand Leake of the United States Public Health Service has adopted the 'Acupuncture' or multiple puncture method with remarkable success. It is interesting to note that both these methods are officially approved and recommended under the New York Regulations. The 'acupuncture' method however is being now generally recognized as about the best. Canada also officially recommends this method to all its vaccinators. In this Presidency however a method recommended to all public vaccinators is of a circular incision by means of a rotatory lancet devised and manufactured in this institute and supplied to all public vaccinators. It consists of a circular disc four millimetres in diameter provided with five tiny conical-shaped needle points. Four of these are on the periphery of the disc and one very slightly longer than the others in the centre. The other end of the lancet is provided with a tiny scoop for placing a drop of lymph on the area to be vaccinated. Through the drop of lymph applied on the skin, the disc end of the lancet, held perpendicularly, is gently pressed and rotated. This, unlike Force's drill method, results in only breaking the skin in a circular incision of just

sufficient depth. Very little oozing of blood is noticed. The central needle point does not as a rule break the skin. Its main function is to fix the lancet and it, being slightly longer than the peripheral ones, serves to press the skin down and thus stretching it helps to cut it more easily by the latter. It will be obvious therefore that such a lancet is absolutely safe in the hands of public vaccinators in India, or at least in this Presidency, who are not qualified medical men. With this lancet they can cut the skin so far and no further. The same could not be said about a knife edge in their hands for vaccination purposes. The knife may be second to none in the hands of medical men, but I do not agree with 'C. L. B.' that it is better than our knuckles in the hands of our vaccinators. This would be best judged by the results of 748,530 primary vaccinations done by the public vaccinators in this Presidency, including Sind, during the year just ended. It is to be particularly noted that all these vaccination operations were done by Belgaum Vaccine Institute pattern of rotatory lancet. The case success rate of these vaccinations is 99.94 per cent, and the insertion success

rate 99.28 per cent. These figures or results will speak for themselves and require no further comments.

In this connection it would be interesting to note the opinion of the International Committee on Smallpox and Vaccination of the Health Organization of the League of Nations in their Report of August 1928. They state:—'The best lymph may have the most different results, according to the manner in which it is used. Next to individual susceptibility, the most important factor is vaccination technique. The Committee does not consider it desirable or even within its province to declare that any particular defined method of vaccination should be exclusively employed by vaccinators in all countries'.

Yours, etc.,
J. L. PINTO, D.P.H.,
Director.

VACCINE INSTITUTE,
BELGAUM,
12th July, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

THE Indian Research Fund Association has elected Major-General J. D. Graham, C.B., C.I.E., R.H.S., Public Health Commissioner with the Government of India, to be its representative on the Imperial Council of Agricultural Research, with effect from the 18th March, 1933, *vice* Lieutenant-Colonel A. J. H. Russell, C.B.E.

To be Honorary Surgeon

Colonel J. P. Cameron, C.S.I., C.I.E., *vice* Major-General W. C. H. Forster, C.I.E., retired. Dated 19th July, 1933.

Colonel H. R. Nutt, V.H.S., Officiating Surgeon-General with the Government of Bombay, is confirmed in that appointment, with effect from the 20th July, 1933.

The services of Lieutenant-Colonel F. A. Barker, O.B.E., Inspector-General of Prisons, Punjab, have been replaced at the disposal of the Government of the Punjab, with effect from the afternoon of the 29th June, 1933.

The Viceroy and Governor-General has been pleased to confirm Major W. R. Stewart in his appointment of Surgeon to His Excellency, with effect from the 18th July, 1933.

On return from leave, Major S. D. S. Greval, an officer of the Medical Research Department is appointed to officiate as Assistant Director, Central Research Institute, Kasauli, *vice* Major Maitra, with effect from the date on which he assumes charge of his duties.

The services of Captain T. J. Davidson are placed temporarily at the disposal of the Government of Burma, with effect from the date on which he assumes charge of his duties.

Captain J. C. Drummond, Civil Surgeon, Midnapore, is posted at the Medical College Hospitals, Calcutta, until further orders.

Captain R. Linton is appointed as Civil Surgeon, Midnapore, *vice* Captain J. C. Drummond, I.M.S.

Subject to His Majesty's approval the undermentioned I.M.S. officers are confirmed in the following order on passing the necessary courses of instructions:

Captains

J. H. Crawford; G. R. M. Apsey.

Lieutenants

J. D. Grant, M.B.
T. E. Palmer, M.B.
W. H. G. Reed, M.A.
W. J. Poole, M.B.
C. J. H. Brink, M.B.

The dates of seniority of the undermentioned Lieutenants (on probation) are antedated to 24th April, 1932—

H. A. Ledgard.
T. F. O'Donnell.
Said Ahmad.
C. C. Kapila.
J. White.

PROMOTIONS

Lieutenant-Colonel to be Colonel

A. H. Proctor, D.S.O., V.H.S. Dated 20th July, 1933, with seniority 1st March, 1928.

Majors to be Lieutenant-Colonels

N. M. Mehta. Dated 26th July, 1933.
G. H. Mahony. Dated 31st July, 1933.
G. Corell. Dated 31st July, 1933.
W. R. Stewart. Dated 31st July, 1933.
H. Chaud, M.C. Dated 31st July, 1933.
V. Mahadevan. Dated 31st July, 1933.
A. C. L. O'S. Bilderbeck. Dated 31st July, 1933.
J. W. Vanreenen. Dated 31st July, 1933.
M. Das, M.C. Dated 31st July, 1933.
J. M. R. Hennessy. Dated 31st July, 1933.
H. H. Brown. Dated 31st July, 1933.
C. H. N. Baker, M.C. Dated 31st July, 1933.
K. R. Rao. Dated 31st July, 1933.

The promotion of Major A. J. D'Souza, M.C., I.M.S., to the rank of Major is antedated to 5th May, 1926.

Captain to be Major

R. McRobert, M.B., Ch.B. Dated the 10th June, 1933.

Captain (on probation) to be Major (on probation)

W. Aitchison, M.C. Dated 20th December, 1932.
(Previous notification on the subject is hereby cancelled.)

LEAVE

Major G. C. Maitra, Assistant Director, Central Research Institute, Kasauli, is granted leave for 8 months, with effect from the 1st August, 1933, or the date from which he may avail himself of it.

RETIREMENT

Lieutenant-Colonel H. A. H. Robson retires from the 1st June, 1933.

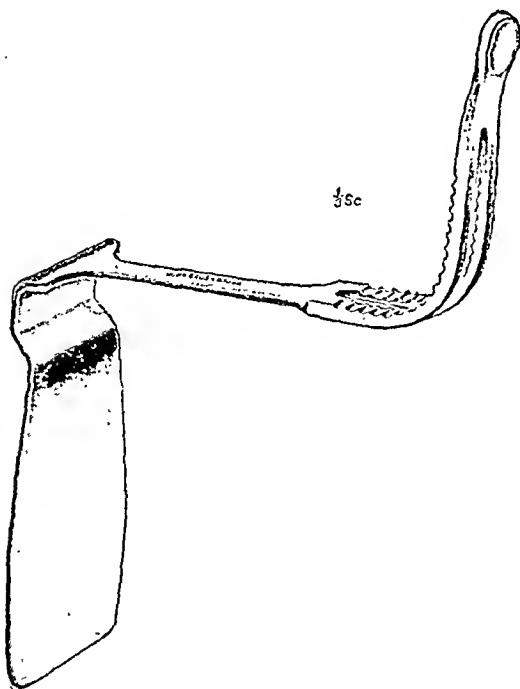
RELINQUISHMENT

Captain (on probation) E. O'Reilly relinquishes his probationary appointment, 20th May, 1933.

Notes

A NEW ABDOMINAL RETRACTOR

This single retractor has been designed for use in operations on the lumbar sympathetic ganglia. It consists of a long, broad blade with a flat, lower margin rounded at the edges, and attached to a shaft at right angles. The handle of the retractor makes an angle of 10 degrees from the vertical at its attachment to the shaft, and is faceted for the reception of the thumb. This angulation is an advantage. When the handle is held vertically, the lower margin of the retractor is inclined



outwards, thus exposing the more deeply lying structures with the minimum amount of pressure on the overlying coils of bowel. At the same time, the hands of the assistant are well away from the wound, and not above it, as they would be were the handle attached at right angles.

R. BROOKE, M.S.

MURANO GLASS

PROFESSORS of laboratories will be interested to know that the well-known Italian factory of Christalleria Murano, Venice, are now represented in India by Messrs. Ezra Brothers, Ruston Buildings, Churchgate Street, Fort, Bombay.

The main qualities of glass manufactured by this factory are:—

(1) *Murano Tenax Glass Tubings*.—This represents neutral glass (hard glass) tubings to be used exclusively for manufacturing ampoules and vials.

(2) *Murano X Glass* is common glass (soft glass) tubings used for manufacturing laboratory apparatus.

(3) *Murano 1922 N Glass*.—It is a neutral heat-resisting glass used for manufacturing laboratory glass. It may be mentioned that the glass has a thermal resistance of 175° Centigrade, the pH constant at 7.1, and its added advantage over the Jena glass is its greater elasticity.

OPERATING THEATRE LIGHTING

THE operating-theatre light fitting is one of the most important items of present-day hospital equipment.

Modern surgery requires adequate lighting, and the selection of a suitable fitting should be carefully made to ensure that the surgeon may work with the maximum of comfort and efficiency. Some form of shadowless lighting has become an essential detail of an up-to-date theatre.

There are many points to consider in the selection of a light fitting and attention is drawn below to some of the important features of G. E. C. operating theatre fittings:

High Light Intensity.—Over 500 feet candles is obtained over a 12-inch circle with a 200 watt OSRAM general service lamp.

Elimination of Shadow.—Light distribution and diffusion of beam ensure minimum of shadow.

Minimum of Heat.—Due to the opaque bottom of the fitting and the hollow cone of light produced, the neck and head of the surgeon are in an area free from direct light and heat.

Colour Correction.—Spectral quality of the light is unaltered. White corrected glass is used for all transmitting and reflecting surfaces throughout the fitting.

Emergency Illumination.—Incorporated in the fitting itself and possessing generally the same characteristics as the main illumination.

Low Running Cost.—No complicated lens system is employed. Standard OSRAM lamps which are inexpensive and easily obtainable are used. Five hours lighting for 1 unit of electricity.

Easy Maintenance.—Quickly removable top and counterweight inspection cover give instant access to lamps, working parts and wiring.

Ease of Cleaning.—The fitting may be easily and quickly cleaned from the theatre floor.

Ease of Adjustment.—Positive in action, the universal adjustment enables light to be directed in any direction at the required angle.

Simplicity of Installation.—Fittings are wired before despatch and have only to be fixed to ceiling and connected to the hospital supply.

Manufacture.—Made in England by the G. E. C. with the best quality British materials throughout.

Price.—Produced at the lowest figure consistent with quality and efficiency.

OIL-SOLUBLE BISMUTH

'STABISMOL' is a solution of a new oil-soluble bismuth compound which has been discovered and manufactured by Boots Pure Drug Co., Ltd. The formula of the compound is bismuth α -carboxy-cyclo-hexanyl acetate.

The drug is supplied in solution in olive oil, and 1 c.cm. of the solution contains 0.1 gramme of bismuth metal. The advantages claimed for this preparation are that it is less painful on injection and more rapidly absorbed than are aqueous suspensions of bismuth salts or of bismuth metal. The superior rate of absorption has been demonstrated by x-ray photographs. Pharmacological experiments have proved the non-toxicity of the compound, and the purity and sterility of the preparation is controlled by analytical and bacteriological tests. The dosage recommended is 2 c.cm. solution (0.2 gramme bismuth metal) weekly.

Messrs. Boots have prepared an interesting brochure which gives full details of the properties of the drug and its mode of administration, and also gives an outline of soluble courses of combined arsenical and bismuth therapy for various types of syphilitic infection. The introduction of bismuth by Sazeras and Levaditi has proved a valuable advance in the therapy of syphilis, but there has been considerable difficulty in finding a satisfactory preparation of this metal. Preparations which form aqueous suspensions are very slowly absorbed, whilst those given in aqueous solution are painful and have often proved to be unduly toxic. This new oil-soluble preparation ought, therefore, to prove a valuable advance in bismuth therapy.

(The British Medical Journal, Vol. I, p. 1011.)

FERRADOL

(A VALUABLE TONIC)

FERRADOL is a new vitamin preparation containing both manganese and iron in a very palatable and diastatically active malt vehicle which Messrs. Parke, Davis and Co. have just introduced. The vitamins A, B and D are all represented in generous quantity in this formula. The vitamin A content of Ferradol is obtained by the inclusion of halibut liver oil which is of such high potency that the small quantity required does not impair the pleasant flavour of this preparation. Vitamin B value is provided by the content, per ounce, of 25 grains of concentrated biologically standardized vitamin B extract from wheat germ and Irradol has been included in sufficient amount to assure a vitamin-D potency of 5D.

Thus Ferradol provides the fat soluble vitamins A and D in larger amounts than a high grade cod-liver oil, the growth-stimulating vitamin B in sufficient quantity, the anti-anæmic effects of iron and manganese and the nutritive and diastatic value of malt.

The malt extract used in Ferradol is nutritious and is an aid to starch digestion. It is made by the vacuum process which protects its enzymatic activity from injury by heat. As a vehicle for the vitamins contained malt extract is ideal. The flavour of the finished product is very pleasing and is, therefore, logically indicated for children who are under-weight, have little appetite or who have not regained normal vitality after some acute infection. Also for adults for the same conditions and during pregnancy and lactation or other periods of stress. A tablespoonful added to the 24 hours supply of the baby's formula will ensure an abundant supply of vitamins A, B and D, will protect against secondary anæmia, and has nutritive value equivalent to approximately 3 ounces of whole milk.

Ferradol supplies 4 calories per gramme or 48 calories per fluid ounce.

Messrs. Parke, Davis and Co. offer this product in 1 lb. cylindrical glass jars.

EMOCAL

An organic calcium preparation for use in pulmonary tuberculosis

For some time the organic compounds of calcium have been utilized for the treatment of tuberculosis. De Renzi has reported that there is a direct connection between the quantity of phosphate of calcium contained in the urine and the loss of flesh of the patients suffering with tuberculosis; and that is, he noticed, that the patient's weight increased or diminished in accordance with the increase or decrease of the salts of calcium eliminated.

To-day it seems that decalcification and the increase of the organic combustion constitute the dominating factors with the battle against tuberculosis. Thus we find that, while the lack of calcium can be considered as the specific and predominating stigma of pre-disposition towards tuberculosis, the calcification of the tuberculous lesions appears to be one of the essential conditions of local cure.

Naturally in regard to therapeutics the organic preparations of calcium should be preferred both because they are more easily assimilated, and because no intolerance whatsoever is met with. Amongst these last-named preparations, I have no hesitation whatsoever in declaring that Zambelletti's EMOCAL is the best because it corresponds in every way to the therapeutical requirements and, besides this, the preparation in question is not eliminated by the emunctory ducts and therefore remains longer in the body thus offering to the latter the maximum therapeutic utilization of the calcium. This preparation is put up in ampoules for intramuscular injection and for intravenous injection. I have always given preference to the latter method since the intravenous injections are exempt from any

inconvenience whatsoever and give the best results more rapidly than the former.

It will, of course, be easily understood that the intravenous injections cannot be continued for a very long time and therefore it is both necessary and useful, after a series of from 15 to 20 intravenous injections, to give the patients another series of intramuscular injections of the same preparation which however do not give rise to any local reactions.

DR. GIACOMO GARGIULO.

The agents for Emocal in India are Stella and Co., Box 868, Bombay.

ELECTRO-MEDICAL APPLIANCES

MALGHAM BROTHERS have written to inform us that Mr. Hirji Malgham is proceeding on a second tour to Europe and will devote considerable time in the well-known factories of The British Hanovia Quartz Lamp Co., Ltd., and Messrs. Schall and Son, Ltd., both in London, makers of the famous Quartz U.V.R. lamps and of pantostats, diathermy units and electro-surgical tissue-cutting apparatus, etc., respectively.

The main idea of this second tour to Europe is to add greater knowledge in the technique of handling electro-medical appliances and to give better and more efficient service than hitherto to the medical profession.

Any member of the medical profession or any hospital requiring first-hand information whilst Mr. Malgham is in Europe will be welcome to write without the least obligation Messrs. Malgham Bros., 20, Western House Road, Bombay.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

Communications on Editorial Matters, Articles, Letters and Books for Review should be addressed to THE EDITOR, *The Indian Medical Gazette*, c/o The Calcutta School of Tropical Medicine, Central Avenue, Calcutta.

Communications for the Publishers relating to Subscriptions and Advertisements should be addressed to THE PUBLISHERS, *The Indian Medical Gazette*, P. O. Box No. 54, Calcutta.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

THE ANÆMIA OF KALA-AZAR

By L. EVERARD NAPIER, M.R.C.S., L.R.C.P.
and

L. R. SHARMA, M.B., B.S., M.R.C.P.E., D.P.H. (Camb.),
D.T.M. & H. (Camb.)

(From the Kala-azar Enquiry, Indian Research Fund
Association, School of Tropical Medicine, Calcutta)

It has always been recognized that a considerable degree of anæmia is the rule in a person suffering from kala-azar. It has also been recognized that when the patient is cured this anæmia disappears, *pari passu* with his return to normal health. But because from a diagnostic point of view there is little significance in this anæmia, a similar degree of erythropenia being present in the majority of the conditions which are likely to be confused with kala-azar, because more valuable diagnostic information may be obtained from the leucocyte counts, and because if the specific disease is cured the anæmia requires no special treatment, clinicians, who pay the most careful attention to the leucopenia, both for making a diagnosis and for gauging progress, have been led to ignore altogether the erythropenia. Even the leading authorities give little attention to this particular aspect of the disease. Rogers (1910) gives a table (unfortunately based on patients in a European hospital) showing that the erythropenia is progressive—not marked in the early stages but becoming 2,500,000 per c.mm. and even less in more advanced cases. Brahmachari (1928) quotes this and adds his own experience that in 7.5 per cent of cases the count is above 4,000,000, in 60.5 per cent between 4,000,000 and 2,500,000, in 24.5 per cent between 2,500,000 and 1,500,000 and in 7.5 per cent below 1,500,000. Knowles (1920) gives the mean for 33 cases as 2,457,270, from 1,416,000 to 3,728,000. Napier (1930) gives the typical blood count in a case of six months' duration as about 3,000,000 and Manson-Bahr (1929) says that the count is often over 4,000,000 and usually over 2,500,000 even in advanced cases.

Little attempt has been made to classify the anæmia, and none to explain its cause. Brahmachari refers to presence of 'poikilocytes, micro- and melagocytes, myelocytes, and erythroblasts' in the peripheral blood. Rogers gives the colour index as 0.65 which he says is about normal for the Assamese on whom this figure was based, and he considers the anæmia to be of the 'pernicious' type, whereas Brahmachari considers that it is more often of the 'chlorotic' type; this suggestion is supported by his finding of a low colour index, but not by his statement regarding the presence of

abnormal cells usually associated with pernicious anæmia.

It is rather surprising that this well-marked and constant departure from the normal has claimed so little of the attention of the investigators in this disease. With the opportunities at our disposal we felt that we should investigate certain points in this aspect of the hæmatology of kala-azar.

It is of course extremely difficult to give a concise account of the blood picture in kala-azar on account of the frequency with which the disease is associated with other infections which must necessarily complicate the picture by introducing contradictory elements. Nearly all our patients in Calcutta have had malaria and are suffering from its after-effects to varying extents; a very high percentage have an ankylostome infection, but few have a heavy enough one to merit the description 'hook-worm disease'; and various concomitant helminthic, bacterial and protozoal infections are frequently encountered. To obtain the most certain and dramatic results with the pentavalent antimony compounds it is advisable to treat these co-existent infections first but in order not to depart too far from 'field' conditions where such a procedure would be impossible we have not usually adopted this plan but have made a practice of treating the kala-azar first and the residual infections, if necessary, afterwards. There is in the majority of cases such a rapid and complete return to normal, despite latent malaria and a mild ankylostome infection, that one is driven to the conclusion that the anæmia is mainly due to the leishmania infection. However, for this enquiry we have chosen patients with no obvious additional infections so as to eliminate, as far as possible, this complicating factor.

The cases were all Indians; the majority had been living in Bengal for years. They were patients in the hospital attached to the Calcutta School of Tropical Medicine. In every case the diagnosis of kala-azar was confirmed by the finding of the parasite.

The total red blood cell count

All authorities agree as to the constant presence of erythropenia, and amongst those who are writing from practical tropical experience there is little difference in their opinion as to the degree of the deficiency. Knowles gives the lowest figures, but his cases had been selected, usually for their severity, and are not a fair sample of the general kala-azar population. We considered the question of collecting and analysing the red blood cell counts from the case notes of patients treated during the last twelve years in the Carmichael Hospital for Tropical Diseases, but we felt that, as these counts had been made by a number of different observers with a number of different (often indifferent) instruments, the results would not

repay the labour entailed and we decided to depend on the counts made during this investigation—which, though comparatively small in number, were made under standard conditions with a good hæmocytemeter—for confirming the observations of other workers.

The counts were made from peripheral blood obtained by pricking the finger. The counts were made about the same time each day and not immediately after a meal. The red blood cell count was done by the usual method with a one-in-a-hundred diluting pipette and a Thoma-Ziess counting chamber. At least 192 squares were counted each time.

As a preliminary measure counts on 10 'normal' Indians, workers in the laboratory, were done; these ranged from 4,775,000 per c.mm. to 6,106,000 and the mean was 5,429,600.

As a further normal control, counts were done on nine patients suffering from dermal leishmaniasis, a condition not usually associated with any general disturbance. The mean of these nine counts was 5,108,000, the lowest being 3,650,000 and the highest 5,957,000; the two patients with the lowest counts were evidently debilitated as they improved considerably during their course of treatment for the skin condition; if these two counts are excluded the remainder fall into line with the other controls.

Of 81 counts done on 47 kala-azar patients before they received specific treatment of any kind the mean was 2,930,395; the highest count was 4,766,000 and the lowest 1,890,000.

It will however be best to take the first count in each case. The mean of these 47 counts is $2,880,000 \pm 54,568$ (probable error). One was below two millions and six were over 3,500,000: that is to say 85 per cent were between these two figures.

Influence of various factors on the blood count

Sex.—The mean of the counts in the eleven female cases was 2,741,000, and in the 36 males 2,922,000.

Age.—The mean of the counts in the seven children under 10 years of age was 2,578,000, in the 13 patients aged between 10 and 20 years it was 2,902,000, and in the 27 adults it was 2,947,000.

Duration of the disease.—The mean of the counts of 13 patients who gave a history of less than six months' duration of illness was 3,042,000; of 18 patients with a history of more than six months but less than a year the mean was 2,871,000; and of the remaining 16 who gave a history of a year or more the mean was 2,757,000.

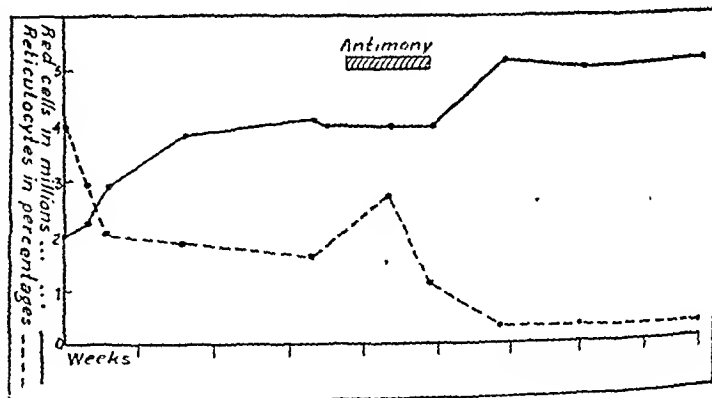
Size of the spleen.—This was less than three inches below the costal margin in 13 cases, the mean of the count in these being 3,003,000; the spleen was three or more but less than six inches in 17, the mean of the count in these being 2,914,000; and in the remaining 16 in which

the spleen was six inches or more the mean of the count was 2,744,000.

Duration of the stay in hospital.—Nearly all the patients were markedly improved by rest in bed and hospital diet alone. Fourteen patients had been in hospital three weeks before the first count was made; the mean of the counts in these cases was 3,344,000, as against a mean of 2,682,000 for the 33 who had been in a shorter time than this.

Conclusions.—The count in young children seems to be lower than in adults, and in females the count is slightly lower than in males. The duration of the disease, as evidenced by the history and the size of the spleen, does not appear to be a very important factor, and the evidence for the steadily progressive nature of the anæmia which Rogers (1910) claimed, is lacking; on the other hand the observations suggest that a moderate degree of anæmia is rapidly acquired and that subsequently this increases very slowly. It is however apparent that the length of the stay in hospital is an important factor. None of these patients had had more than symptomatic treatment, e.g., purgatives and cough mixtures, but they were all on a full diet. This diet was in most cases better than the patients received in their own homes; in the case of the poorer class patients because they could not afford a better diet, and in other cases because it is a common practice in Bengal to 'starve a fever'. The chart given below is an extreme example; this woman came

FIG. 1



Note improvement in count prior to any treatment

from a well-to-do household but had been kept on a very low diet for some time.

The reactions of the red blood count under various forms of treatment will be discussed below.

The reticulocyte count

A reticulocyte count was made on each occasion with the red cell count. The technique adopted was as follows:—

Technique.—The slides were carefully cleaned by immersion in sulphuric acid and potassium bichromate solution, subsequently washed in running water and finally in distilled water. One side was marked, and then polished with jewellers' rouge. The slide was then

dipped in a 0.75 per cent solution of brilliant cresyl blue in absolute alcohol, and transferred rapidly to a cylindrical specimen bottle at the bottom of which had been placed a piece of filter paper, and the cork replaced in the bottle. The slide is allowed to stand upright in this bottle until it is dry. This ensures slow drying and an even distribution of the film of dye. A suitable sized drop of blood obtained from a finger prick is taken on to a specially cleaned cover-slip, $\frac{3}{4}$ by $1\frac{1}{2}$ inches, which is immediately dropped on to the stain-covered slide. The drop of blood is of such a size that when very gentle pressure is applied to the cover-slip the blood just fails to reach the edge. The edges are now sealed with paraffin wax which is melted and applied with the aid of a match.

An Ehrlich's eye-piece or some similar device is used to restrict the microscopic field. A succession of fields is then counted, the total number of red cells, the number showing reticulation noted and the percentage calculated; the actual numbers are then calculated from the total red cell count which was done at the same time.

At the beginning of the investigation we adopted the practice of counting as reticulocytes only those cells in which there was definite reticulation, not counting those in which there were only a few isolated dots taking the stain. This accounts for the fact that our 'normal' counts are lower than those found by the majority of observers. Later, we noted down both the number of young reticulocytes (the definitely reticulated cells) and the older reticulocytes (those showing isolated dots only); we found that in the kala-azar cases the young reticulocytes constituted about 60 per cent of the total reticulocytes, but that often after treatment it was possible only to find older reticulocytes. The figures we give in this paper refer to young reticulocytes only, unless it is stated otherwise, so that for comparing our counts with those of other workers about 40 per cent should be added to our figures.

Normal controls.—Counts were done on 10 healthy Indian males, laboratory workers. 1,500 to 2,000 red cells were counted in these as the counts were low. The counts varied from 0.1 per cent to 0.63 per cent, the mean being 0.42. The mean actual number of reticulocytes was 22,790 per c.mm.

Of the nine cases of dermal leishmaniasis the mean reticulocyte percentage was 0.67 and the mean reticulocyte count 34,224 per c.mm.

Kala-azar cases prior to any treatment.—The mean reticulocyte percentage in 82 counts in 47 cases was 2.07 per cent; only one was over 4 per cent, 13 were over 3 per cent, 36 between 2 and 3 per cent, 27 between 1 and 2 per cent, and six under 1 per cent. Two counts only were below the mean normal, i.e., 0.42, and these were both in the same case.

The mean of the reticulocyte counts was $60,743 \pm 1,593$ (probable error) per c.mm. There were 10 counts over 80,000, the highest being 137,000, and only four under 30,000, so that 82.9 per cent of the counts were between these two figures. The same two low counts (from one case) were the only ones below the mean normal count.

Abnormal red cells.—No nucleated red cells were observed in the whole series. There was no marked poikilocytosis or polychromasis, and, although there were differences in the sizes of

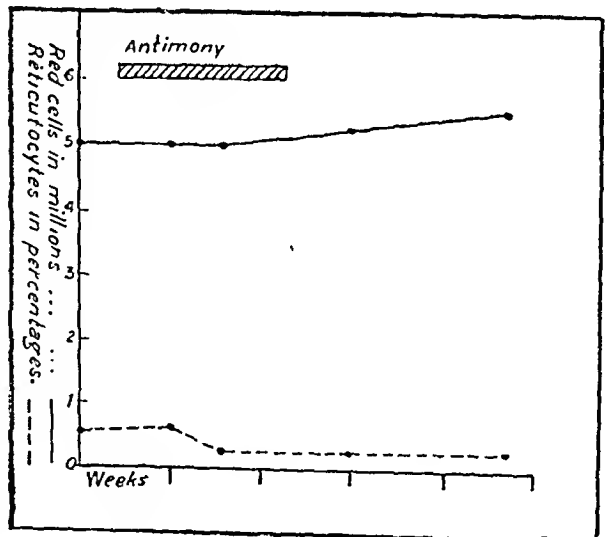
the red cells, no frank microcytes and few macrocytes were seen.

The effect of antimony treatment

Controls.—We could not very well keep a normal man in hospital for some weeks and subject him to a course of neostibosan injections, so we took three cases with only dermal lesions as controls. One of these was a hospital patient whose red blood count had risen from three and a half to five millions before treatment was given; 17 days after the completion of a course of 12 daily injections it rose to 5,400,000 and the reticulocyte count which had been 30,000 fell to 12,000. In another the counts, which were originally within the normal limits, fell slightly, but still remained within the normal limits. In a third case there was a distinct rise in the red cell count, from 4,125,000 to 5,125,000, during a course of about two months in which injections were given twice a week. She was an out-door patient throughout, and had no other treatment, but her general condition improved; it is of course possible that the effect was a psychological one, consequent on the disappearance of the disfiguring skin lesions; the reticulocytes fell from 36,000 to 10,000 during the same period.

It is evident that the antimony injections do not have any marked and immediate effect on the red cell or reticulocyte counts. A typical chart is given.

FIG. 2



A case of dermal leishmaniasis

Kala-azar cases.—There were 12 cases in which antimony treatment only was given; in two of these the red blood cell count was just over four millions, in six it was between three and four millions, and in the other four it was between two and a half and three millions. The reticulocyte count varied between 0.72 and 3.14 per cent. In most instances two counts before and two counts during treatment were

done; the means of the counts are given below :—

TABLE I

Antimony treatment only; means in 12 cases

Relationship to treatment	Red cells per c.mm.	Reticulocyte per cent	Reticulocytes, actual number per c.mm.
Before ..	3,258,000	1.59	51,802
During ..	3,364,000	1.09	36,668
After 1st week	4,208,000	0.49	20,619
2nd week	4,313,000	0.32	13,802
3rd week	4,589,000	0.30	13,767

Two characteristic graphs are also given.

FIG. 3

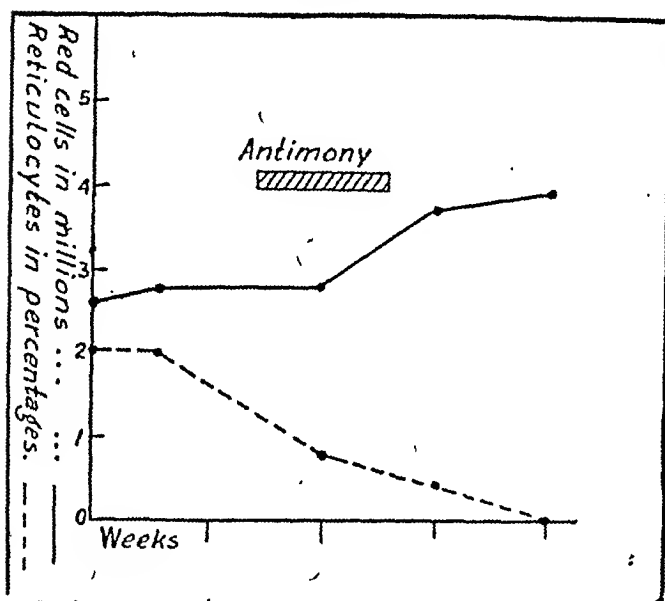
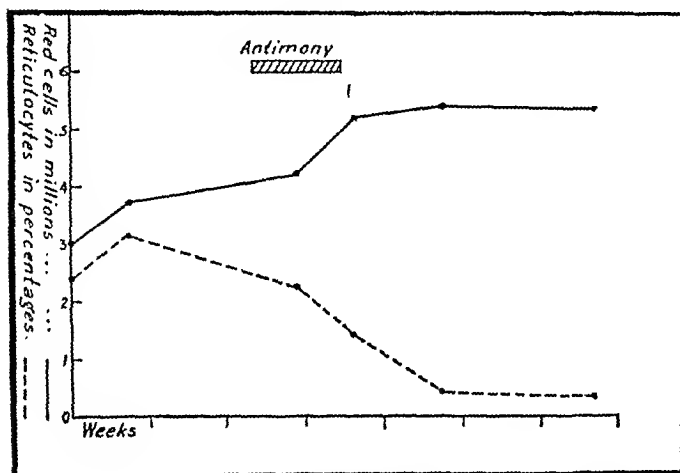


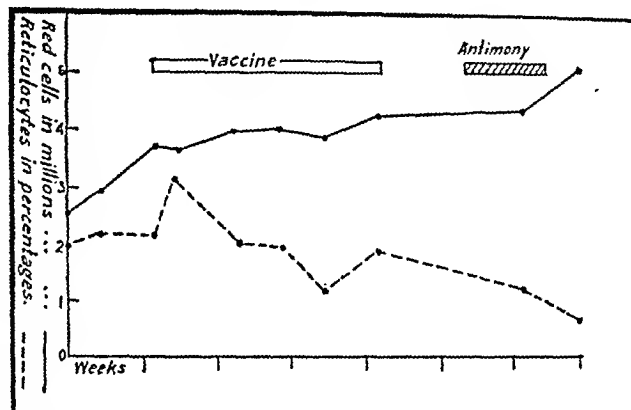
FIG. 4



It will be seen that from the commencement of treatment there was a fall in the reticulocytes, but the increase in the total red cells did not occur until the first week after the treatment was finished. The reticulocytes continued to fall and by the time the patient was discharged they had in every case fallen to less than 0.6 per cent, and in some no reticulocytes could be seen in a dozen fields.

Three other patients were given experimental vaccine treatment. There is no reason to suppose that in any instance did this treatment have any beneficial effect on the course of the disease; in two there was no appreciable effect on the red cells or the reticulocyte count until the course of neostibosan was given. The graph of the third case is given below; it will

FIG. 5



be seen that there was a slight improvement in the red blood count during the vaccine course, but that this count had already been rising before and that the antimony treatment, when it was eventually given, had the usual and immediate effect of improving the red blood count and reducing the reticulocytes.

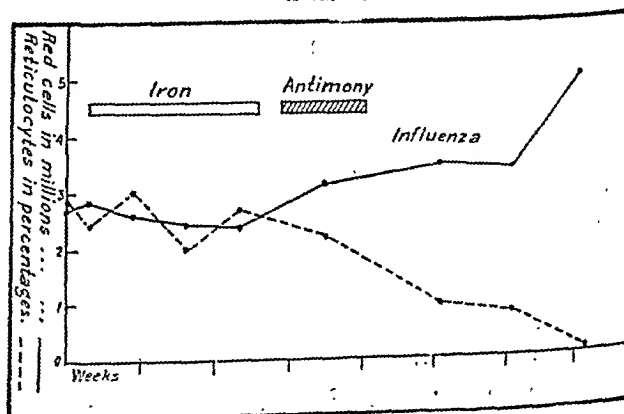
In the cases already referred to, the patients responded well clinically to treatment, but in one case there was no such clinical response. In this case there was no improvement in the red cell count, and though the reticulocyte count fell slightly, it still remained above normal.

The effect of the administration of other therapeutic agents

With the object of obtaining some clues as to the mechanism of anaemia in kala-azar, we administered to our patients a number of different therapeutic agents that are of value in the treatment of various forms of anaemia.

Iron.—In five cases large doses of iron were given. This was usually ferri et ammonii citras in doses of twenty grains three times a day. The red blood cell count prior to treatment in all these cases was between two and a half and three millions. During the iron

FIG. 6



administration both the reticulocyte count and the red blood count tended to fall, but with the administration of neostibosan the reticulocyte count fell sharply and the total red cell count immediately started to improve; the final rise in the number of reticulocytes was due to a sharp rise in one case. The means of the five cases are given below in tabular form:

TABLE II
Iron treatment

Relationship to treatment	Red cells per c.mm.	Reticulocyte per cent	Reticulocytes, actual number per c.mm.
Before ..	2,698,000	2.70	72,846
During iron treatment—			
1st week	2,557,000	2.04	52,163
2nd week	2,356,000	1.70	40,032
3rd week	2,403,000	1.53	36,766
During antimony	2,972,000	1.27	37,744
After antimony—			
1st week	3,405,000	0.88	29,961
2nd week	3,603,000	0.46	16,574
3rd week	4,681,000	0.76	35,576

The graph of a typical case is also given.

Liver therapy.—Intravenous hepatex was given in four cases. The doses, 1.5, 3.5, 5 c.cms., etc., were given on successive days. Three, three, four and seven doses were given, respectively. During and after the administration of hepatex frequent (at 48 hours intervals) blood counts were done in order not to miss any reticulocyte crisis that might occur. One of the patients who had three doses of hepatex was very debilitated; her red blood count, 3,125,000, tended to fall slightly, but her reticulocyte count which was just over 60,000 fell to below 6,000 on the fifth day from the commencement of the treatment and never rose again. On the tenth day the patient, who had been in a collapsed condition for twenty-four hours, died; she did not suffer from any complicating infection to account for her sudden death and no post-mortem examination was allowed. In the other cases there was a slight downward tendency of both the red cell and the reticulocyte counts during and after the hepatex administration, but the usual reaction followed the administration of antimony. A graph of a typical case and a table showing the means of these four counts are given below; the figures for 'during' and 'after' treatment refer to only three cases.

FIG. 7

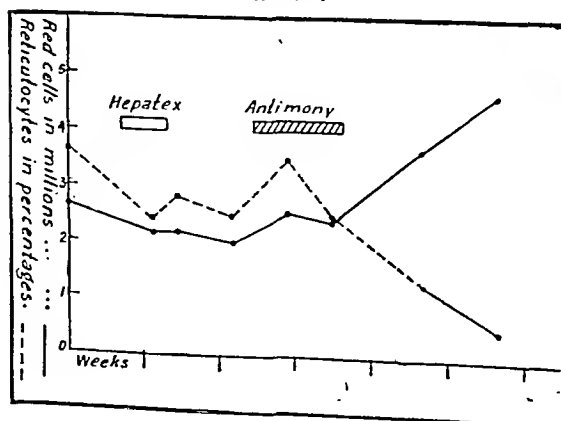


TABLE III
Liver treatment

Relationship to treatment	Red cells per c.mm.	Reticulocyte per cent	Reticulocytes, actual number per c.mm.
Before ..	2,887,000	2.48	71,598
During hepatex	2,721,000	2.10	57,141
After hepatex	2,534,000	1.81	45,865
During antimony	2,662,000	2.37	63,089
After antimony—			
1st week	2,813,000	1.65	46,414
2nd week	3,728,000	1.31	48,837
3rd week	4,275,000	0.89	38,047

Another patient was given liver extract by the mouth. His red cell count was 2,000,000 and his reticulocyte count 64,000 (3.2 per cent) before he took the liver extract; the former underwent little change during the liver treatment but later, when the course of neostibosan was given, it fell sharply to below a million and then rose again very slowly to 2,500,000. The reticulocyte count rose to 99,000 during the liver treatment, fell again to 27,000 and then again rose sharply to 105,000. At this stage the patient was obviously not cured from a clinical point of view and a further course of injections were prescribed, but we were not able to follow the course of the blood picture further in this case. This was the only case in which there was a rise in the reticulocytes that in any way resembled a reticulocyte 'crisis', but, even making allowances for our different standard for judging reticulocytes, it could not be compared with the reticulocyte rise that occurs in cases of pernicious anemia following liver administration.

Marmite.—Six patients were given marmite for two to three weeks soon after admission. In one case there was a slight fall in both the red cell and in the reticulocyte counts; in four there was a slight rise but this did not amount to more than is usual in all cases after admission; but in one there was a very distinct rise in the red cell count, from two and a half millions to four millions. In no case was there a reticulocyte 'crisis'; in one case there was a rise from 75,000 to 120,000, but in the others there was a slight rise or a slight fall. On the administration of antimony the patients reacted in the usual way. A table showing the means of the six counts is given, and also a typical chart.

FIG. 8

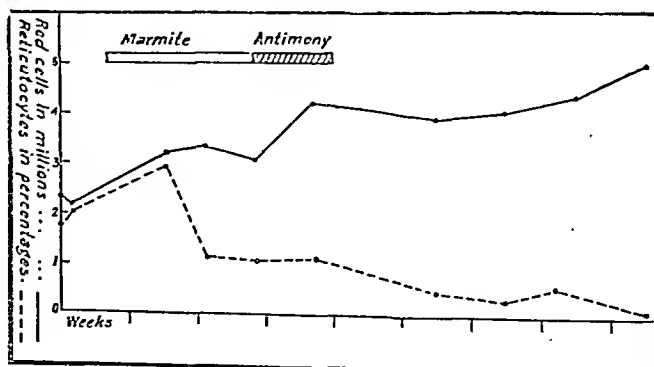


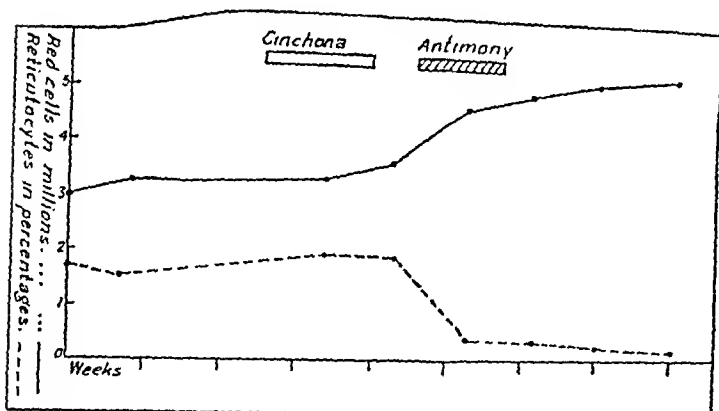
TABLE IV
Marmite

Relationship to treatment	Red cells per c.mm.	Reticulocyte per cent	Reticulocytes, actual number per c.mm.
Before any treatment.	2,703,000	2.16	58,384
During marmite—			
1st week	3,045,000	2.26	68,817
2nd week	3,287,000	1.95	64,095
During antimony	3,495,000	1.75	61,162
After treatment—			
1st week	3,994,000	1.05	41,937
2nd week	4,074,000	0.57	23,222
Final ..	4,436,000	0.20	8,872

Bcmax.—One patient was put on this food on account of the reputed high vitamin-B content. There was a slight increase in his red cell count and a slight fall in the reticulocytes.

Cinchona alkaloids.—In two cases in which scanty malarial parasites were found in the peripheral blood, quinine and cinchona febrifuge, respectively, grains 10, twice daily, was given. In one case the fever was controlled temporarily, in the other it was not affected. In neither case did the alkaloid have any effect on the red cell or reticulocyte counts; in both, the administration of neostibosan led to a rapid return towards normal. A chart of one case is given below.

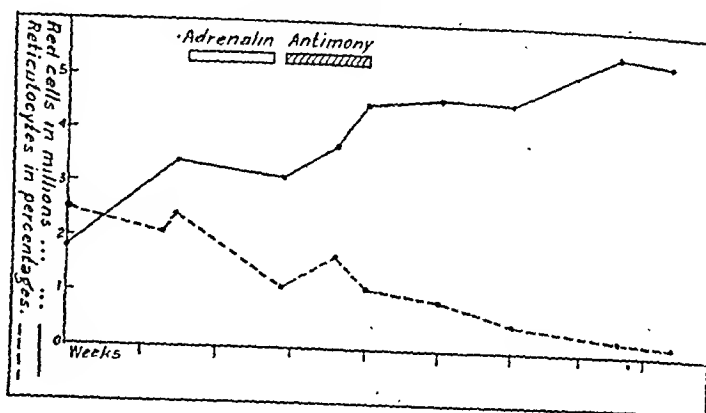
FIG. 9



Adrenalin.—Adrenalin has been said to have a stimulating effect on the bone marrow, and, in view of the fact that there is evidence of hypoadrenia in kala-azar, we gave four patients a course of injections of adrenalin, 0.5 c.cm. of a 0.1 per cent solution daily for a week to 10 days.

There is no evidence that these injections had any effect on the red cell or reticulocyte counts. A table is given below showing the means of the counts before any treatment, after the adrenalin course was completed, and during and after the antimony course. The apparent rise in the count after the adrenalin is due to general improvement in the patients after admission; in only one out of four cases was there a rise between the last count before adrenalin and the first count after adrenalin. There was, if anything, a slight fall in the reticulocyte count following adrenalin. The counts behaved in the usual way after neostibosan was given. A characteristic chart is shown.

FIG. 10

TABLE V
Adrenalin

Relationship to treatment	Red cells per c.mm.	Reticulocyte per cent	Reticulocytes, actual number per c.mm.
Before ..	2,864,000	2.50	71,600
After adrenalin	3,361,000	1.66	55,793
During antimony	3,740,000	1.59	59,466
After antimony—			
1st week	3,866,000	1.17	45,232
2nd week	4,980,000	0.34	16,959
Final ..	5,054,000	0.30	15,162

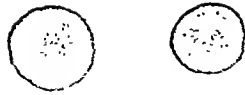
Hæmoglobin

Napier (*loc. cit.*) gives the hæmoglobin percentage ('based on European standards') as 60 and the colour index as 1 in a typical case of kala-azar of six months' duration.

Rogers' statement that the colour index is 0.65 and that this figure is about normal for the Assamese is difficult to understand and to correlate with his further statement that the anæmia is usually of the pernicious type. Brahmaehari (*loc. cit.*) writes 'The average colour index in this series of cases is 0.64, and in nearly 10 per cent of them it was nearly equal to the average normal in Indians'. The difficulty in understanding the meaning of these statements can to a certain extent be accounted for by the confusion that exists regarding the meaning of the expressions 'hæmoglobin percentage' and 'colour index'. The only satisfactory definition of the former is 'the number of grammes of hæmoglobin in 100 cubic centimetres of blood', though by it most writers mean the percentage hæmoglobin compared with an arbitrary normal the hæmoglobin value of which they fail to state. The colour index is necessarily a relative figure and is best arrived at by working out the normals for males from the class from which the patients are drawn and making unity the normal index.

The usual clinical methods of estimating hæmoglobin are notoriously unsatisfactory, and, as at the beginning of the investigation no very

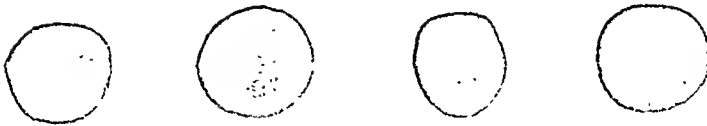
PLATE X



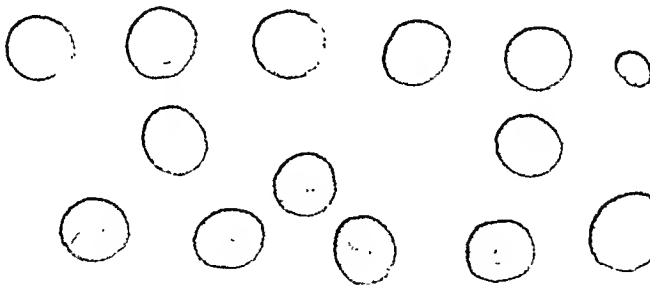
1



2



3



4



Mullick

5

Human blood.

1. Normal red cells.
2. Reticulocytes older forms.
3. Reticulocytes young forms.

Hamster blood.

4. Reticulocytes.
5. Normal red cell.

satisfactory method had been adopted by us for rapid estimation of the hæmoglobin, this was not made as a routine measure. However, a rough estimation was usually made by means of the ordinary Tallqvist scale. In 15 cases this estimation was checked by the readings with a Fleischl-McIsheer hæmoglobinometer and the necessary corrections made in the rest of the readings. Thus, a high degree accuracy cannot be claimed for all these observations but they are probably as accurate as any so far published; the results are therefore recorded.

Of 63 observations in 32 cases before any treatment whatsoever was given, the maximum was 11.25 grammes of hæmoglobin per 100 c.cm. of blood and the minimum 4.2 grammes. The mean was 7.08 grammes and the probable error 0.084.

Of 28 observations made on 28 patients just before they were discharged as cured the maximum was 15 grammes, the minimum 8.25 grammes and the mean 12.01 grammes per c.cm. of blood.

Colour index.—Taking the normal hæmoglobin of the patient class as 15 grammes and the normal red blood cell count as 5,400,000, we estimated the colour index before treatment as from 0.65 to 1.08, with a mean of 0.885, and at the time of discharge as from 0.847 to 1.21 with a mean at 1.005.

The size of the red cells

For estimating the mean size of the corpuscles Eve's halometer was used. The estimation was made in 22 cases before any treatment was given and at the time the patient was discharged cured. Before treatment the mean was 7.559μ and at the time of discharge 7.375μ . Using the same instrument the same observer made 50 estimations in 10 normal Indians, obtaining a mean of 7.216μ .

Fragility of the red blood cells

This was tested with different strengths of sodium chloride by one of the usual methods. A number of normal bloods were first tested; the means of the concentration at which hæmolysis commenced was 0.427 per cent and at which it was complete was 0.36 per cent.

The estimation was made in 35 cases before treatment and in 23 of these, before, during and after treatment. The room temperature was usually between 33°C . and 28°C . In nearly every instance the cells were found to be more resistant than normal to hæmolysis; in one case only did hæmolysis commence and in only two was it complete at a higher salt concentration than is the case in normal bloods. After treatment the fragility returned to normal. The means of the readings are given below in tabular form.

TABLE VI

	Hæmolysis commenced	Hæmolysis complete
Before treatment	0.3913	0.3321
During "	0.4100	0.3573
After "	0.4236	0.3636
Normal control	0.4266	0.3616

The fragility of the reticulocytes

The reticulocyte percentage was estimated in a tube in which no hæmolysis occurred and in the last tube in which submaximal hæmolysis occurred. It was found in the cured cases and controls that the percentages were about equal or, if anything, the percentage was lower in the tube in which some hæmolysis had occurred, but in cases prior to treatment there was a marked increase in the tube where partial hæmolysis had occurred, indicating that the reticulocyte in kala-azar is more resistant than the older red cell.

The Arneth count

The count was done in 30 kala-azar cases before treatment: the mean of the Arneth indices was 92.67. In 10 cases only was it done again after treatment. The means of these 10 counts before and after treatment, and the means of the Arneth indices are given below:—

Groups	I	II	III	IV	V	Index
Before treatment	49	36	12	3	0	91.8
After "	34	38	19	8	1	81.3

It is apparent that there is a very marked shift to the left and that the count had not returned to normal at the time the second count was done. The personal factor must play an important part in the working of this count; in this case control counts on normal persons showed that the writers had a tendency to make counts with a higher Arneth index than normal, but there can be no doubt there is a very marked shift to the left in kala-azar cases, as the fact was confirmed for us by an independent worker.

Other investigations

Urobilinuria.—The urine was examined qualitatively for urobilin in 39 cases before treatment and, in the majority of these, during and after treatment. The results were given as 'no definite increase', 'definite increase', 'marked increase' and 'very marked increase'. In nine cases no definite increase was noted on the first examination, but in two of these there was an increase at the time of some subsequent examination prior to treatment; that is to say a definite increase was demonstrated in 32 (or

82 per cent) cases before treatment. The table shows the findings summarized:—

TABLE VII
Urobilinuria

	First examination before treatment	During treatment	After treatment	Examination one month to six weeks later
Very marked increase.	18	13	13	1
Marked increase	3	10	5	1
Definite increase	9	7	5	2
No increase of urobilin.	9	5	9	3

Four cases in which no urobilin was found before showed a definite increase after or during treatment, and in three cases, in which there was definite increase before, there was none after treatment. In the fourth column of the table only those cases in which there had been a very marked increase throughout are included; it will be seen that in some the urobilin persisted for a long time.

Lævulose-tolerance test

This was done in six cases before treatment and in four of these after treatment. The results were within the normal limits, except in one case prior to treatment; in this case after the administration of 25 grammes of lævulose there was a rise from 75 to 96 milligrammes per 100 c.cm. in the blood-sugar, and the level was maintained at about 90 for two hours.

The van den Bergh test

This was done in five cases; in four of these it was done both before and after treatment. The 'direct' reaction was negative throughout. The 'indirect' reaction was positive in four and doubtful in the fifth before treatment, but negative after treatment. These cases were included in the six in which the lævulose-tolerance test was done; in all of them there was urobilinuria, both before and after treatment.

Summary of the observations

Red cell count.—The mean of the first counts in 47 cases of kala-azar was 2,880,000 per cubic millimetre and the probable error of this mean $\pm 54,568$. In only one case was the count below two millions, and in six it was above three and a half millions. In 34 subsequent counts on some of these patients prior to treatment the mean was 3,000,000. The counts were lower in women, and in children they were lower than in adults.

Duration of the disease did not appear to influence the count very much, but the length of time the patients had been in hospital seemed

to be an important factor. The blood count improved without treatment in nearly every case; better food was probably the cause of this improvement. Abnormal red cells were not noted in any of the 47 cases.

Reticulocyte count.—With the technique and criteria we adopted the normal was 0.42 per cent, or 23,000 reticulated cells per c.mm.

Before treatment in 82 counts in 47 patients the mean percentage was 2.07; the mean of the count was 60,743 per c.mm. and the probable error of this mean $\pm 1,593$.

The effect of antimony treatment.—The administration of neostibosan was always followed by a sharp fall in the reticulocytes and an increase in the red cell count; at the end of the third week after treatment the mean red cell count had risen to 4,589,000 and the mean reticulocyte count had fallen to 13,767 per c.mm.

Administration of other therapeutic agents.—The effect of the administration of iron, liver, marmite, adrenalin, and the cinchona alkaloids was tried. In the case of marmite there was a slight, but doubtful-significant, improvement in the red cell count; in no other case was there any significant improvement in the blood picture. In no instance was there a reticulocyte crisis, and in most cases the reticulocyte count fell slightly. In every instance the red cell and reticulocyte counts reacted in the characteristic way on the subsequent administration of antimony.

Hæmoglobin.—Before treatment the mean of 63 observations on 31 patients was 7.08 grammes per 100 c.cm. of blood and the probable error of the mean ± 0.084 gramme, the maximum was 11.25 grammes, and the minimum 4.20 grammes.

After treatment and just prior to discharge, the mean of 28 observations on 28 patients was 12.01 grammes per 100 c.cm. of blood, the maximum was 15.00 and the minimum 8.25.

Colour index.—Taking the normals as 15 grammes and 5,400,000, respectively, the mean index was 0.885 before treatment and 1.005 at the time of discharge.

Halometric readings.—Mean size before treatment was 7.559 μ , and after 7.216 μ .

The fragility of the red cells.—The resistance of the red cells to the action of hypotonic saline was increased prior to treatment, but it returned to normal after treatment.

The Arneth count.—There was a very marked shift to the left in all cases before treatment; this shift was still apparent after treatment, but had been modified; the means of the Arneth indices before and after treatment were 91.8 and 81.3, respectively.

Urobilinuria.—There was a distinct increase in the urobilin present in 32 out of 39 cases before treatment, and in 36 out of 39 at some time during the course of the disease. In the majority of cases there were large quantities present throughout the course of the disease,

and for some weeks after treatment was completed.

Liver function tests.—In only one out of six cases was there any evidence of levulose intolerance prior to treatment; in this case the blood-sugar rose by 21 milligrammes, and remained above normal for 24 hours. After treatment no intolerance was demonstrable. In four out of five cases the van den Bergh 'indirect' reaction was positive before treatment, and in the fifth the reaction was doubtful. The 'direct' reaction was negative throughout, and the 'indirect' reaction was negative in all cases after treatment.

Discussion

This does not claim to be a complete investigation of the anæmia of kala-azar; there are many lacunæ which other workers will perhaps fill. Nevertheless, we have thought it worth while to summarize our findings and examine them to see if we can draw any conclusions as to the nature of this anæmia, more especially as the opportunity for continuing the investigation does not at present exist.

It is clear that in kala-azar there is a remarkably constant anæmia; it is more or less normocytic (the halometer readings being only slightly above normal) and it is hypochromic. It does not react to the common hæmatinic agents that we gave, nor does significant improvement follow the treatment of complicating factors such as malaria (it should perhaps be explained that in no instance during the investigation did we encounter a patient suffering from a hook-worm infection sufficiently large to suggest that this helminthic infection was causing any significant anæmia), but it reacts almost immediately to pentavalent antimony, the specific for this disease.

It is justifiable to assume that the production of anæmia is a part of the morbid process in kala-azar, but it is a matter for discussion as to how the anæmia is brought about. For purposes of discussion let us take this simple classification of anæmias:—

(a) the true secondary anæmias due to loss of whole blood from the skin, mucous or serous surfaces; this loss may be acute or chronic,

(b) anæmias due to errors in erythrocytogenesis; these may be due to

(i) aplasia or hypoplasia of toxic, nutritional, or obstructive mechanical origin,

(ii) dysplasia; these are mainly deficiency anæmias which may be macrocytic or microcytic according to the stage at which hæmopoiesis is interfered with,

(c) anæmias due to errors in erythrolysis; these again can be divided into anæmias

(i) due to defects in the red cells themselves caused by parasitization or the effect of poison, or of congenital origin,

(ii) hyper-function of the reticulo-endothelial tissues responsible for the disposal of obsolete red cells.

It is obvious that the anæmia cannot be a true secondary anæmia, (a) in our classification, because although small hæmorrhages from mucous membranes are common, they are not a constant occurrence.

Melleney has pointed out that kala-azar is essentially an infection of the reticulo-endothelial system, and he and other workers have shown that in the bone marrow in this infection there is a marked increase in the histiocyte tissue, replacing the fat and eventually the normal hæmatopoietic tissue. This invasion of the bone marrow commences early in the infection, but at first it does not appear to interfere much with the blood-forming elements; the invasion is, however, progressive and in the rib marrow in human cases it appears eventually to displace the hæmatopoietic tissue completely. Such a state of affairs must eventually bring about anæmia of the hypoplastic kind, and hitherto this has been accepted as the explanation for the leucopenia and anæmia characteristic of kala-azar; there are, however, certain points to be considered. Firstly, the leucopenia and the erythropenia appear early in the infection and are not essentially progressive, whereas at this stage the amount of replacement of hæmatopoietic tissue is not serious and the reserves of the hæmatopoietic system are known to be very large; secondly, the moderate reticulocytosis and the marked shift in the Arneeth count to the left do not suggest a hypoplastic origin; and, thirdly, there are certain other observations, such as the evidence of increased hæmolysis, which require explanation.

It has been suggested that the anæmia might be an aplastic anæmia of toxic origin, but the evidence of the presence of any toxin in leishmania infections is very slender. There is evidence that the anæmia is increased by a low dietary, but improvement is slight and can only be brought up to a certain point by increasing the diet.

Again the evidence that it is not a dysplasia due to some deficiency (*e.g.*, Castle's intrinsic factor, vitamins, or iron) cannot be said to be complete as the possibilities are inexhaustible but we failed to get any significant improvement—evidenced either by an increased red cell count or by a reticulocytosis—with our trials in supplying the most likely deficiencies, and furthermore the anæmia disappeared on the administration of antimony alone which cannot be classed as an essential factor for hæmatopoiesis.

On the other hand there is considerable evidence of increased red cell destruction. There was in almost every case a moderate but definite reticulocytosis, much the same degree of reticulocytosis that occurs in a moderately heavy malarial infection, where it is definitely

known that red blood cells are destroyed. There was again a constant very marked urobilinuria and an 'indirect' van den Bergh reaction, evidence of increased hæmolysis and/or inability of the liver parenchyma cells to metabolize the products of hæmolysis. There is no histological evidence that the parenchyma cells of the liver are damaged in the uncomplicated case of kala-azar, and the lack of evidence of lævulose intolerance and the fact that the 'indirect' van den Bergh reaction rapidly becomes negative after treatment, all tend to indicate that the urobilinuria is due to excessive hæmolysis rather than hepatic deficiency.

The excessive hæmolysis provides a stimulus for increased erythropoiesis which is evidenced by the reticulocytosis. On the administration of antimony this increased destruction ceases and with it the stimulus for increased production also, so that the organism, being attuned to a blood supply with a lower oxygen-carrying capacity than normal, ceases to demand an excessive hæmatopoiesis, which then continues more or less normally until the normal number of red blood cells have been provided.

The evidence of the existence of a toxin, which might be held responsible for this hæmolysis, is lacking, and there is no parasitization of the red cells, as is the case in malaria, nor is there any other defect in the red cells to account for the increased hæmolysis. Our fragility tests indicate on the contrary that the red cells are tougher than normal, which suggests that the combing out of obsolete or defective blood cells is more thorough in this disease than it is in normal man, that is to say, there is a hyperactivity of the normal mechanism of erythrolysis. This is conceivable in view of the fact that marked proliferation of the cells of the reticulo-endothelial system—the system concerned in erythrolysis—is the characteristic feature of generalized leishmania infection.

We cannot here go into the question of the mode of action of antimony in this disease, but our observations (Napier, Krishnan and Lal, 1933) suggest that antimony acts through the reticulo-endothelial system, possibly in this case by paralysing the newly-formed reticulo-endothelial cells so that they can no longer phagocytose red cells; this would lead to the death of the contained parasites and the cells themselves would eventually become lysed. If this occurred one would expect the immediate cessation of excessive hæmolysis and the slower disappearance of urobilinuria, which would naturally continue until the parasitized reticulo-endothelial cells had all been lysed and the products of this excess metabolism had been excreted; there is evidence that this does occur.

By way of conclusion we can say that there is some evidence that the anæmia of kala-azar is caused by increased erythrolysis, and it is suggested that this may be a direct result of

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THE TOXICITY OF TETRACHLORETHYLENE TO CATS

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and

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FOLLOWING the successful use of tetrachlorethylene in other parts of the world in the treatment of hookworm infection, Maplesstone and Mukerji (1929) tried this drug in Calcutta, but they came to the conclusion that it was not so efficient as carbon tetrachloride and that it also appeared to be just as toxic as the latter drug, and therefore its use was discontinued at the Calcutta School of Tropical Medicine. Recently, however, we have been led to modify somewhat this opinion, so it was decided to give tetrachlorethylene another trial. The work of Lamson, Robbins and Ward (1929) clearly showed that tetrachlorethylene is not so toxic to animals as is carbon tetrachloride, but on account of the surprisingly fatal effects of the latter on cats in Calcutta, a fact which was demonstrated by Chandler and Chopra (1925), and which was not in agreement with the findings of American pharmacologists, it was considered advisable to test tetrachlorethylene also on Calcutta cats before using it again in the treatment of human beings. This work has now been done, and as the same methods of administering the drug were employed in this investigation as were employed with carbon tetrachloride by Chandler and Chopra, the results of their experiments and those of the present

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the general increase in the tissue and blood histiocytes—the characteristic reaction to the leishmania infection.

Acknowledgments

Our thanks are due to Dr. A. K. Mukerji for taking the halometric readings, and to Dr. J. P. Bose for doing the van den Bergh and lævulose-tolerance tests.

REFERENCES

- Brahmachari, U. N. (1928). *A Treatise on Kala-azar*. London: John Bale, Sons and Danielsson, Ltd.
Knowles, R. (1920). *A Study of Kala-azar*. *Indian Journ. Med. Res.*, Vol. VIII, p. 140.
Manson-Bahr, P. H. (1929). *Manson's Tropical Diseases*. Ninth Edition. London: Cassell and Co.
Napier, L. E. (1930). *Leishmania*. In the *Handbuch der Pathogenen Mikroorganismen* by Kolle, Kraus, Uhlenhuth and Wassermann. Band VII, Lfg. 47, p. 1497. Jena: Gustav Fischer.
Napier, L. E., Krishnan, K. V., and Lal, C. (1933). *Cytological Studies of the Blood and Tissues in Kala-azar and Associated Conditions*. Part V. *Indian Med. Gaz.*, Vol. LXVIII, p. 75.
Rogers, L. (1910). *Fevers in the Tropics*. London: Henry Frowde.

series of tests with tetrachlorethylene form a useful basis for comparison of the effects of the two drugs.

Tetrachlorethylene both in milk and in water was given to cats but no difference in the type or severity of symptoms was observed in the two series. The commencing dose of tetrachlorethylene employed was 0.5 c.cm. per kilogramme of body weight. This dose was gradually increased and no cat exhibited any unusual signs at all until a dose of 1 c.cm. per kilogramme was reached. At this stage the cats exhibited giddiness, restlessness, drowsiness and a certain amount of unsteadiness in the hind limbs, but they completely recovered by the third day after treatment. Similar symptoms of varying severity, which depended on the size of the dose of tetrachlorethylene, were noted in all the cats until the dose of 4.5 c.cm. per kilogramme was reached, and they all recovered within three days. When doses of 5 c.cm. per kilogramme were reached all the cats died, usually within twenty-four hours of the drug being given, but one cat lingered in a semi-conscious state for nine days before death. The urine in the bladder of this animal contained a large amount of albumen, red blood cells, pus cells and casts. Larger doses than 5 c.cm. per kilogramme could not be given as the cats invariably vomited all or part of the dose every time this amount was exceeded.

We gave cats doses of 2 c.cm. and 3 c.cm. respectively of tetrachlorethylene per kilogramme of body weight, mixed with 4 c.cm. of 95 per cent alcohol, and this experiment was repeated twice. None of the cats showed any greater signs of intoxication than those in which it was given in milk or water. It seems clear that alcohol is not a contra-indication to the use of this drug.

Chandler and Chopra (1925) in their experiments with carbon tetrachloride on cats found that with such a small dose as 0.5 c.cm. per kilogramme, forty-five out of forty-nine cats died, and that with a dose of 0.25 c.cm. twenty-four out of twenty-seven died. These results alone indicate that the toxic effect of carbon tetrachloride is much greater than that of tetrachlorethylene.

According to Lamson, Robbins and Ward (1929) tetrachlorethylene has no destructive action on either the liver or kidneys, for they examined one hundred and sixteen animals including dogs, puppies, cats, rabbits and mice that had been given doses ranging from 0.3 c.cm. to 25 c.cm. per kilogramme without finding any change except a certain degree of fatty metamorphosis in the livers of cats and puppies, which they regard as a more or less normal condition for these animals. At the same time it should be noted that they killed cats and dogs with doses as small as 4 c.cm. per kilogramme though other dogs survived repeated dosing over long periods with 4 c.cm. per

kilogramme as well as still other dogs which were not killed by much larger single doses, so these results are not conclusive. In all cases they consider death was due to an over-dose of a hypnotic, though they do not explain how this occurred in adult dogs which they say do not absorb the drug from the intestine.

Dr. M. N. De, Professor of Pathology, Medical College, Calcutta, kindly examined sections of the livers and kidneys of several cats that had been given doses of tetrachlorethylene ranging from 1 c.cm. to 4.5 c.cm. per kilogramme and were killed within forty-eight hours of being given the drug. He also examined the organs of two cats that died within forty-eight hours of receiving doses of 5 c.cm. per kilogramme. The summary of his detailed report is as follows:—

Liver.—Congestion and fine fatty change, and a small amount of necrosis in one case.

Kidneys.—Congestion in the glomeruli with albuminous exudation, in the cats receiving the higher doses. Granular and fatty change in the tubular epithelium, the amount of damage being proportionate to the size of the dose.

From these results it seems clear that tetrachlorethylene has a definitely damaging action both on the liver and kidneys of cats, but comparison with the pathological findings of Chandler and Chopra (1926), on similar cats given carbon tetrachloride, indicates that the reaction of both these organs to the latter drug is so much more intense that the two drugs are not really comparable from this point of view. The much greater toxicity of carbon tetrachloride is still further emphasized when it is remembered that 0.5 c.cm. per kilogramme of this drug causes incomparably greater damage than does 5 c.cm. per kilogramme of tetrachlorethylene.

These experiments suggest that the effect of tetrachlorethylene on human beings in therapeutic doses will be negligible because 1 c.cm. per kilogramme in cats produces nothing more than a slight congestion in both liver and kidneys, and a dose of 3 or 4 c.cm. in the average Indian weighing sixty to seventy kilogrammes would at most represent only 0.15 c.cm. per kilogramme.

Conclusion

Tetrachlorethylene is much less toxic than carbon tetrachloride, and in therapeutic doses it causes no damage to the organs of otherwise healthy animals. An added advantage of tetrachlorethylene over carbon tetrachloride is that apparently it can be given in alcohol without increasing its toxicity.

REFERENCES

- Chandler, A. C., and Chopra, R. N. (1925). The Toxicity of Carbon Tetrachloride to Cats: A Warning. *Indian Med. Gaz.*, Vol. LX, p. 406.
Chandler, A. C., and Chopra, R. N. (1926). Effects of the Administration of Sugar, Magnesium Sulphate, (Continued at foot of next page)

A COLORIMETRIC METHOD FOR THE DETERMINATION OF MILK PROTEINS

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THE method is based on comparing the blue colours developed by adding Folin's (1922) phenol reagent to different samples of milk and to a standard tyrosin solution. Of the different amino acids, only tyrosin and tryptophane (Folin and Looney, 1922) have been shown to give rise to a blue colour with this reagent; and tryptophane has been found to give rise to 58 per cent of the colour developed by an equal amount of tyrosin. We have determined colorimetrically the tyrosin equivalents of milk proteins for cow and buffalo milk, and these factors enable one to find out quickly the protein percentage of any sample of cow or buffalo milk.

The method is that followed by Greenberg (1929) for estimating the blood serum proteins. In the case of milk however, a turbidity and slight precipitation always result after the addition of the phenol reagent; this leads to slight modifications of technique.

By a series of colorimetric experiments and parallel determinations of the protein contents by Kjeldahl's method, we find that, on an average, 12 milligrammes of cow milk proteins and 15.2 milligrammes of buffalo milk proteins correspond respectively to 1 milligramme of tyrosin.

The following notes may be useful.

Reagents required :—

- (1) 5 N. NaOH.
- (2) Standard solution (0.02 per cent) of pure dry tyrosin in 0.1 N (approximately) HCl.
- (3) Folin's phenol reagent (Folin and Ciocalteu, 1927).
- (4) Whatman's filter paper, no. 5, size 15 centimetres.

For a series of milk samples take the corresponding number of marked measuring flasks. Arrange a similar number of marked filter funnels and beakers.

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Sodium Citrate and Dilute Acid on the Liver Damage Done by Carbon Tetrachloride. *Indian Journ. Med. Res.*, Vol. XIV, p. 219.

Lamson, P. D., Robbins, B. H., and Ward, C. B. (1929). The Pharmacology and Toxicology of Tetrachlorethylene. *Amer. Journ. Hyg.*, Vol. IX, p. 430.

Maplestone, P. A., and Mukerji, A. K. (1929). Tetrachlorethylene in the Treatment of Hookworm Disease. *Indian Med. Gaz.*, Vol. LXIV, p. 424.

Rinse the pipettes twice with the sample after thoroughly shaking and mixing it, and pipette off 0.2 c.cm. of each sample in the case of cow's and buffalo's milk into the corresponding measuring flask and 4 c.cm. tyrosin solution into a separately marked flask. Add about 25 c.cm. of water to each, washing down all the traces of milk or tyrosin solution. Add 2 c.cm. of 5 N. NaOH to each, gently shake, add more water and again shake. Add 3 c.cm. of the phenol reagent and fill up to the mark as quickly as possible with water. Shake and keep for 10 minutes. Filter, and after 5 minutes of filtration begin to take colorimetric readings of different samples and complete all the readings within 15 minutes, i.e., from 15 minutes to within half an hour after the addition of the phenol reagent.

This time factor is important, as the maximum colour develops in about 15 minutes and after some time begins to fade.

When taking successive samples in the same colorimeter cup, rinse it twice with the solution under examination and wipe the colorimeter tube dry with a filter paper before immersing it into a fresh sample in the cup. The tyrosin standard is taken in the right-hand cup and fixed at 20, and the left-hand cup with the sample is adjusted till the colour matches, when the reading is taken.

Most of the experiments have been done in duplicate.

Samples should be fresh and examined colorimetrically preferably within 4 hours. Sour milk gives unreliable readings.

The protein content is calculated from the formula :—

$$\text{Protein percentage} = \frac{R}{X} \times T \times \frac{100}{S} \times \frac{F}{1,000}$$

where R = the arbitrary reading of the standard, i.e., 20.

X = the reading of the unknown.

T = tyrosin content in milligrammes of the standard, i.e., 0.8 in 4 c.cm. which we take.

S = the aliquot part of the milk used in c.cm.'s (0.2 c.cm. in this case).

F = the factor of tyrosin equivalence of the particular milk proteins (cow = 12, buffalo = 15.2).

Substituting actuals the formula reduces :—

$$\text{Protein percentage} = \frac{8 \times F}{X}$$

Taking the value of F for cows to be 12, and for buffaloes to be 15.2, this formula simplifies into :—

$$\text{Protein percentage} = \frac{96}{X} \text{ (for cow's) and } \frac{121.6}{X} \text{ (for buffalo's).}$$

The determination of 'F' for cow's milk.

TABLE I

Experiment number	Reading of the sample	Actual protein percentage by Kjeldahl's	F (calculated)
1	30.9	2.87	11.0
2	28.4	3.15	11.2
3	25.0	3.8	12.06
4	29.1	3.6	13.0
5	28.2	3.6	12.69
6	30.1	3.06	11.5
7	27.4	3.6	12.33
			83.78
			Average = $\frac{83.78}{7} = 12$.

TABLE II

Showing comparison of results (1) colorimetrically taking $F = 12$ and (2) by Kjeldahl's method

Cow's milk

Experiment number	Reading of the sample (x)	Protein percentage (96) X	Protein percentage by Kjeldahl's method
1	31.0	3.1	3.2
2	26.5	3.6	3.5
3	32.0	3.0	3.2
4	25.5	3.76	3.8
5	29.1	3.29	3.3
6	23.46	4.09	4.02
7	30.16	3.18	3.38
8	25.7	3.7	3.6
9	25.76	3.7	3.9
10	23.0	4.2	4.0
11	29.8	3.2	3.1

TABLE III

Buffalo's milk

Determination of F for buffalo's milk

Experiment number	Reading of the sample	Protein percentage by Kjeldahl's	F (calculated)
1	26.45	4.5	14.85
2	27.55	4.53	15.6
3	23.86	4.78	15.0
4	24.6	5.13	15.8
5	26.5	4.66	15.43
6	23.0	5.2	14.95
7	27.3	4.4	15.0
8	24.4	4.8	14.64

Taking an average $F = 15.2$.

TABLE IV

Showing results calculated colorimetrically and those determined by Kjeldahl's method

Experiment number	Reading of the sample	Protein percentage by Kjeldahl's	Protein percentage by Kjeldahl's
1	24.7	4.9	4.8
2	24.2	5.0	4.7
3	31.0	3.9	3.8
4	25.4	4.8	4.78
5	23.3	5.2	5.3

Human milk

0.4 c.cm. milk was used for each colorimetric experiment.

TABLE V

Showing the protein percentage obtained by Kjeldahl's method and 'F' calculated on colorimetric readings and protein percentage

Experimental number	Reading of the sample	Protein percentage by Kjeldahl's	F (calculated)
1	22.8	1.79	10.18
2	33.26	1.4	11.6
3	23.0	2.68	15.4
4	28.2	2.01	14.38
5	37.5	1.4	13.1
6	27.5	1.96	13.47
7	23.1	2.5	14.4
8	20.6	2.9	14.93
9	24.4	2.4	14.6
10	26.6	2.1	13.96
11	25.4	1.8	11.43
12	24.1	2.1	12.65
13	23.8	2.2	12.09
14	26.4	2.2	14.5
15	17.8	2.6	11.57
16	20.8	1.97	11.2
17	24.0	2.5	15.0
18	28.8	1.8	12.96

Taking the average $F = \frac{237.47}{18} = 13.2$.

These samples came from women of various nationalities, of different ages, and different serial orders of pregnancies. They are all however from parturient women during the first week of lactation. The protein shows a wide variation in content. Lowenfeld, Widdows, Bond, and Taylor (1927) showed that the average percentage of protein in human milk varies considerably during lactation and the same authors found that the first month of lactation is a period during which the protein content falls from a high to a low percentage.

The calculated value of F in column 4 shows variations from 10.18 to 15, suggesting that the tyrosin and tryptophane content of human milk varies considerably in the first week of lactation. The calculated average for $F = 13.2$ is evidently not a close one and, as might be expected, the values obtained colorimetrically in table VI are not in close agreement with actual Kjeldahl findings. The method is therefore not suitable for determining the protein of human milk during the first week of lactation. We had no opportunities to examine human milk after the first week of lactation.

TABLE VI

Human milk

Showing colorimetric findings and actual protein percentage by Kjeldahl's method

Experiment number	Reading of the sample	Protein percentage by Kjeldahl's	Protein percentage by Kjeldahl's
1	21.0	2.5	2.1
2	26.0	2.0	1.6
3	26.9	2.0	1.7
4	24.2	5.0	4.7

The percentage calculated colorimetrically is that by volume, whereas Kjeldahl's determination gives percentage by weight. For practical

purposes this difference may be neglected as it is a difference only in the second place of decimals.

The percentage of milk proteins has been made a standard by the Madras Food Adulteration Act, 1918, and the validity of such a standard has been verified by Stewart and Chatterjee (1931) in Calcutta samples of milk. A simple method which can be completed within half an hour, with very small samples, either individually or in a series, may be useful.

In the case of known cow and buffalo milks reliable results can be obtained.

Our thanks are due to Lieut.-Col. Boyd, Principal of the Medical College Hospitals, and Lieut.-Col. Gow of the Eden Hospital for supplying samples of human milk from the Eden Hospital. We thank Mr. P. C. Mitra for supplying pure samples of cow's and buffalo's milk.

REFERENCES

- Folin, O. (1922). *Laboratory Manual of Biological Chemistry*. New York: D. Appleton and Co.
 Folin, O., and Ciocalteu, V. (1927). *Journ. Biol. Chem.*, Vol. LXXIII, p. 627.
 Folin, O., and Looney, J. M. (1922). *Ibid.*, Vol. LI, p. 421.
 Greenberg, D. M. (1929). *Ibid.*, Vol. LXXXII, p. 545.
 Lowenfeld, M. F., Widdows, S. T., Bond, M., and Taylor, E. I. (1927). *Biochem. Journ.*, Vol. XXI, p. 1.
 Stewart, A. D., and Chatterjee, N. K. (1931). *Indian Med. Gaz.*, Vol. LXVI, p. 320.
 Widdows, S. T., Lowenfeld, M. F., Bond, M., and Taylor, E. I. (1930). *Biochem. Journ.*, Vol. XXIV, p. 327.

THE ACTION OF SOME SYNTHETIC ANTIMALARIAL REMEDIES ON THE UTERUS

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QUININE, until a few years ago, was considered to be the only effective remedy against malaria, and competent authorities expressed the opinion that it would be culpably trifling to use any other drug but quinine in the treatment of serious cases of malaria. The shortage of quinine supply during the war led to the production of a number of synthetic compounds for the treatment of malaria. Of these atebirin and plasmoquin have been shown to have a definite effect on the malarial parasites and have come to stay as powerful antimalarial agents. The work carried out in the School of Tropical Medicine, Calcutta, on the action of these drugs on the Indian strains of malaria parasites is in accord with findings obtained in other parts of the world.

Plasmoquin has been tried by a large number of workers, and in India, Napier, Butcher and Das Gupta (1932) used it with success in their field experiments. Atebrin has been found by Napier and Das Gupta (1932) to destroy the asexual stages of the malarial parasites especially of subtertian malaria. Chopra, Das Gupta and Sen (1933) have reported very favourably on the effectiveness of this compound against infections with the different strains of malarial parasites met with in Bengal. The antimalarial properties of tabetren and malarcan, two closely allied drugs, are under investigation and they show promise of being effective. These drugs are eupreine compounds and therefore cinchona derivatives.

In view of the favourable results obtained by these newer remedies and of the practical clinical importance of their oxytocic properties, it was decided to make a study of their action on the uterus. In this investigation direct observations were made on the action of these drugs on the movements of the isolated as well as the intact uteri of animals. The results obtained, although they may not be totally applicable in human beings, will give a fair indication as to the general action these drugs may be expected to produce in pregnant patients under treatment.

Plasmoquin is said to be n-diethyl-amino-isopropyl-8-amino-6-methyl-quinoline. The drug was synthesized by Professor Schulmann in the Bayer-Meister Lucius Laboratory, Elberfeld, and its antimalarial property confirmed by Roehl. Its action on the uterus as worked out at Elberfeld showed that in concentrations of 1 in 100,000 to 1 in 50,000, it produced no effect on the isolated uterus of the guinea-pig. In animal experiments *in situ*, the uterus did not respond to intravenous injections of 0.05 mgm. per kilogramme of body weight, but a response was obtained with doses twenty times this amount, which would be very toxic, the therapeutic dose being 0.3 mgm. per kilogramme of body weight. Clinically the effect of plasmoquin in pregnancy was studied by Jensen who treated successfully a pregnant woman suffering from malaria. Mazumdar (1929) stated that plasmoquin does not induce uterine contractions during pregnancy. Thakkar (1929) treated multiparæ in the third, fifth and eighth months of pregnancy with daily doses of 0.06 gm. of this drug. Manson-Bahr (1932) considered that plasmoquin is well tolerated by pregnant women and that they go on to full term and give birth to healthy children. Epstein (1933) states that, in therapeutic doses, plasmoquin has probably no action on the human uterus.

Atebrin is the dihydrochloride of an alkyl-amino-alkyl-amino-acridine derivative which was synthesized by Mietzsch and Mauss. It is a yellow powder soluble 1 in 14 of water, and has a very bitter taste. Apart from a

record by Manson-Bahr (1932) who treated successfully a pregnant woman, systematic study of its action on the uterus has not been made.

Malarean and tabetren are compounds of some stereo-isomeric bases of methyl eupreine with methyl acridine chloride and hydrochloric acid. The former was elaborated in the laboratory of pharmaceutical chemistry, Neugersdorf, and the latter by Messrs. Howard and Sons, London. Their effectiveness against malaria is being investigated by the senior author.

Experimental

Our experiments were carried out on the uteri of cats, rabbits and guinea-pigs. The action on the isolated uteri was studied in a Dale's bath containing Fleisch's solution at a temperature of 37.5°C. which had an hydrogen-ion concentration varying from 7.4 to 7.6, and through which oxygen was bubbled at an uniform rate. The action *in situ* was studied on cats by a modification of Barbour's method described by Chopra and David (1927).

As pure plasmoquin powder could not be obtained, tablets were employed in these experiments. One of these was dissolved in dilute hydrochloric acid, the acid was neutralized with caustic soda till precipitation just started, and in this way the drug was held in solution. For experiments with atebren, ampoules containing 1 c.cm. of the compound in 10 per cent solution were employed. The ampoules of malarean used in these experiments each contained 1 c.cm. of solution containing approximately 3 grains of the drug.

PLASMOQUIN. Isolated uterus.—In dilutions of 1 in 200,000 the automatic movements of the isolated uteri of cats and rabbits are accelerated and the tone of the muscle is increased. Higher dilutions such as 1 in 300,000 to 1 in 400,000 sometimes produce these results but often they are inert. Isolated uterus treated with successive concentrations of plasmoquin such as 1 in 200,000, 1 in 100,000, 1 in 50,000, reacted by showing a larger and larger acceleration of the automatic movements and an increase in the tone of the musculature as the strength was increased. With repeated doses no paralytic effects were obtained on the muscle. On the virgin uterus of the cat, effective concentrations varied from 1 in 200,000 to 1 in 100,000. In a few experiments with the pregnant uterus of rabbits, concentrations of 1 in 200,000 and more increased the tone of uterine movements, the response being greater as the pregnancy advanced. On the isolated uterus of the guinea-pig concentrations of 1 in 50,000 accelerated the rhythm and the amplitude of the contractions; no increase in the tone of the musculature was observed. Concentrations of 1 in 30,000 to 1 in 20,000 produced a decided increase in the tone.

Uterus in situ.—With doses of 2 mgm. per kilogramme, a slight increase in the tone and frequency of the contractions was observed; smaller doses produced no effect whatever. In multiparous cats doses of 1 mgm. per kilogramme increased the amplitude of individual contractions in some cases. After paralysis of the sympathetic nerve-endings with ergotoxin, the effect was still obtained showing that the drug probably acted on the musculature.

ATEBRIN. Isolated uterus.—On the non-pregnant isolated uterus of cats and rabbits concentrations of 1 in 100,000 to 1 in 50,000 were necessary to produce any appreciable increase in the amplitude of contractions,

and even with these concentrations the tone of the musculature was not materially altered. Gradually increasing concentrations of atebren after repeated washing of the uterus always produced a definite increase in the amplitude of contractions, thus showing no marked deleterious effect on the musculature. On the virgin uterus of the cat, concentrations of 1 in 20,000 to 1 in 10,000 were necessary to produce any definite response. With concentrations of 1 in 10,000 of the drug there was a definite increase in the tone and also acceleration of the rhythm. A few experiments were also performed on the pregnant uterus of rabbits; concentrations of 1 in 200,000 to 1 in 100,000 distinctly augmented the amplitude of the individual contractions, but no increase in tone was observed. On the isolated guinea-pig's uterus such high concentrations as 1 in 20,000 produced an increase in the amplitude of the contractions; 1 in 10,000 only increased the tone of the muscles.

Uterus in situ.—Doses from 1 to 2 mgm. per kilogramme of body weight, which fall within the therapeutic limit, had no effect whatever on the parous uterus. Increase in tone and acceleration of the rhythm was obtained with doses of 3 to 4 mgm. per kilogramme of body weight and a dosage of 5 mgm. per kilogramme increased both the tone and the rhythmic movements and produced a great fall of blood pressure. The effects on the virgin uterus were not materially different.

MALAREAN and TABETREN.—As already pointed out these are closely allied compounds and the effects produced on the uterus by both were more or less the same.

Isolated uterus.—Concentrations of 1 in 50,000 and less had no effect whatever. Stronger solutions such as 1 in 20,000 increased the tone in some cases; in others only the amplitude of the contractions was increased. On the virgin uterus of cats concentrations in the neighbourhood of 1 in 10,000 were necessary to obtain a definite response. On the pregnant uterus of rabbits acceleration of rhythm and slight rise in tone were observed with concentrations such as 1 in 30,000; with successive doses of higher strengths the uterus goes on to a state of tonic contraction. The rhythmic movements of the uterus of the guinea-pig were only increased with such concentrations as 1 in 5,000; marked increase in tone was obtained with 1 in 1,000.

Uterus in situ.—On the multiparous uterus, doses of 4 to 5 mgm. per kilogramme of body weight produced augmentation of individual contractions; increase in tone of the musculature was observed in some experiments. On the virgin uterus doses smaller than 6 to 7 mgm. per kilogramme had no effect whatever. After paralysis of the sympathetic nerve-endings with ergotoxin, the uterus still reacted in the same way.

QUININE.—In order to compare the effects of these drugs with quinine, a series of experiments were also performed at the same time with the bihydrochloride.

Isolated uterus.—Concentration of 1 in 200,000 in these experiments increased the amplitude of individual contractions of the parous uterus of the cat and the rabbit without any increase in tone; weaker concentrations, such as 1 in 300,000, produced no effect whatsoever. On the virgin uterus of the cat, concentrations varying from 1 in 150,000 to 1 in 100,000 produced a slight increase in both the tone and rhythmic movements; weaker concentrations, e.g., 1 in 200,000, increased the amplitude of individual contractions without enhancing the tone. The uterus of guinea-pigs definitely responded by accelerated contractions to concentrations of 1 in 20,000; concentrations in the neighbourhood of 1 in 10,000 markedly improved the tone.

Uterus in situ.—The smallest dose of quinine which could elicit a definite response in the virgin uterus of a cat was 5 to 6 mgm. per kilogramme of body weight; it definitely increased both the tone and amplitude of contractions. In a multiparous uterus doses between 3 to 4 mgm. per kilogramme produced a definite increase of tone and acceleration of the rhythmic movements. Smaller doses were absolutely ineffective.

Discussion

Acton and Chopra (1925) showed that with doses of 0.1 gm. of quinine by the mouth in cats weighing 2.5 kilogrammes, a concentration of 1 in 150,000 to 1 in 100,000 was reached in the blood in half an hour. An analysis of results obtained in these experiments shows that plasmoquin stimulates the contractions in concentrations of 1 in 200,000 or thereabouts in the isolated uterus. It would not be possible to attain such concentrations in the blood with the doses that are usually employed. Two mgm. per kilogramme given intravenously was the average smallest dose which increased the force of uterine contractions; this means that for an average individual 50 to 60 kilogrammes in weight, about 100 to 120 mgm. of plasmoquin will be necessary to produce any noticeable effect. The effective therapeutic dose of plasmoquin, however, never exceeds 20 mgm. for a single administration. It would therefore appear that in therapeutic doses plasmoquin will in all probability have no effect on the contractions of the human uterus gravid or otherwise.

Atebrin has been found to increase the amplitude of contractions of the isolated uterus only in concentrations in the neighbourhood of 1 in 50,000; improvement in tone and increase in the amplitude of contractions of the intact uterus was observed with intravenous doses of 4 mgm. per kilogramme of body weight. Such big doses invariably produced a fall of blood pressure which might possibly account for the effects produced on the uterus, but as these effects were also observed on the isolated uterus it is possible that the drug acts directly on the uterine muscle. Considering that the intravenous dose of atebrin, which would produce definite increase in uterine contractions, is 4 to 5 mgm. per kilogramme in the cat, the corresponding dose in human beings would work out at 240 to 300 mgm. But the effective therapeutic dose of atebrin never exceeds 100 mgm. at a time for an average adult man, so this falls within the range of safety.

With regard to malarcan and tabetren it has been observed that doses of 4 to 5 mgm. per kilogramme produce augmented contraction in the multiparous uterus while in the virgin uterus 6 mgm. or more have to be employed. This effect is not abolished even after paralysing the sympathetic nerve-endings with ergotoxin and therefore these preparations must act directly on the uterine muscle. The question arises whether these drugs will have any action on the human uterus in the doses that are usually given. Tabetren is prescribed in doses of 2 tablets of 3 grains each (approximately 400 mgm.) at a time, every four hours until 60 such tablets are given. Malarcan is prescribed every 2 hours so that the patient receives 12 tablets daily. For an average individual 250 to 300 mgm. of these drugs will be necessary to

produce any effect on the uterus and as the effective dose of both malarcan and tabetren is about 400 mgm. it is possible that even in therapeutic doses they may stimulate uterine contractions. Moreover as these remedies are to be given repeatedly six times a day the chances of cumulative action are greater.

If the effects produced by these drugs are compared with those produced by quinine, it will be observed that acceleration of uterine movements in the cat is possible by quinine in doses of 5 to 6 mgm. per kilogramme which is equivalent to 300 to 360 mgm. (about 5 grains) for an adult human being, 50 to 60 kilogrammes in weight. With the usual therapeutic doses in man therefore the margin of safety with plasmoquin and atebrin would appear to be very much greater than with quinine, malarcan and tabetren.

A perusal of the above results shows that the pregnant uterus is much more sensitive to the action of all these drugs than the virgin and parous uterus. Of all the drugs tested, plasmoquin and atebrin in therapeutic doses are least likely to produce any untoward effects on the pregnant uterus; malarcan and tabetren are more likely to stimulate uterine contractions if given in doses not much larger than therapeutic doses.

Summary and conclusions

1. The pregnant uterus is much more sensitive to the action of the antimalarial drugs than the non-pregnant uterus.

2. Our experiments on animals indicate that plasmoquin and atebrin, in therapeutic doses, are not likely to produce oxytocic action on the pregnant human uterus.

3. Malarcan and tabetren may produce increased contractions of the pregnant uterus in doses not very much larger than therapeutic doses. The chances of oxytocic action are increased in view of the fact that these preparations have to be given repeatedly every 2 or 3 hours throughout the course of treatment.

4. Large therapeutic doses of quinine are likely to increase the contractions of the pregnant uterus, and therefore in pregnancy small doses (e.g., 5 grains) repeated every 4 or 5 hours should be prescribed.

REFERENCES

- Acton, H. W., and Chopra, R. N. (1925). The Concentration of Quinine in the Circulating Blood. *Indian Journ. Med. Res.*, Vol. XIII, p. 197.
- Chopra, R. N., Das Gupta, B. M., and Sen, B. (1933). Atebrin in the Treatment of Indian Strains of Malaria. *Indian Med. Gaz.*, Vol. LXVIII, p. 425.
- Chopra, R. N., and David, J. C. (1927). The Pharmacological Action of Quinine. *Indian Journ. Med. Res.*, Vol. XV, p. 343.
- Epstein, D. (1933). The Action of Plasmoquine on the Uterus. *Quart. Journ. Pharmacy and Pharm.*, Vol. VI, p. 5.
- Mazumdar, A. R. (1929). Some Observations on Plasmoquin. *Journ. Trop. Med. and Hyg.*, Vol. XXXII, p. 47.

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BILIARY LITHIASIS

Part I.

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It is scarcely justifiable to consider biliary lithiasis apart from other gallbladder conditions, owing to the close association between the infective process and stone formation.

As in other surgical conditions, the treatment of biliary lithiasis must be based on an intimate understanding of the ætiological, anatomical, mechanical and pathological factors all considered together; it would be wrong to consider the mere existence of stones as a reason for removing the gallbladder without taking into account the cause of stone evolution. Yet this seems to be the basis of the present-day treatment of gallstones by either cholecystectomy, or the more palliative cholecystotomy. Nor is sufficient regard paid to the post-operative symptoms which frequently follow removal of the gallbladder.

Let us review in brief the ætiology, pathology and the anatomy of the biliary tract, with a view to the treatment of these factors as they arise.

Ætiological factors.—There are several classifications of gallstones, but we will consider them under two main headings: aseptic and septic.

Aseptic stones may be formed from pure cholesterol or pure bilirubin, or, rarely, biliverdin; or from a mixture of these, in any proportion. They all result from metabolic disturbance with an increase of the 'mother' pigment circulating in the blood. For example, the excessive cholesterol saturation of the blood during pregnancy leads to an excessive secretion of that salt by the liver, and this, passing in large quantities to the gallbladder, is precipitated either by crystallization, or because there is lack of the solvent salts in the bile. Once the cholesterol is precipitated, it tends to sediment to the fundus of the gallbladder by gravity, where it accumulates on account of the deficient outlet through the normal passage. If this precipitated cholesterol is removed from the gallbladder in the fine state of subdivision in which it is deposited when freshly formed in the biliary tract, no solidification occurs. For the solidification of the precipitate it is necessary that it should be retained sufficiently long, and this

may be brought about by any obstruction in either the cystic duct or Hartman's pouch. Aseptic stones are formed in the gallbladder itself as pure cholesterol or pure bilirubin stones, and there is now no doubt that such pure stones may be found also in the hepatic radicles of the biliary tract. This latter fact disposes of the main argument for the removal of the gallbladder for the cure of the source of their formation. Further, the common bile duct may be the seat of stricture following upon the impaction of previous stones, or an injury inflicted during the operation of cholecystectomy, and the same difficulties would follow.

The much-quoted statement that stones are a precursor of cancer is also an incomplete argument for removal of the gallbladder. We do not remove the urinary bladder or the kidney for stone; if the kidney is removed for stones it is because they recur there or because one kidney has sustained damage, and never because cancer is feared. But even if we accept the cancer-precursor idea, cholecystectomy leaves the site of stone impaction in the common bile duct, which could equally be the seat of cancer when irritated. It seems more reasonable to remove possible irritation at this site by the consideration of the other factors, removing by less drastic and more efficient technique the cause of stone formation or recurrence. Radically removing the site of stone formation finds a parallel in destroying a house as a prophylactic against cholera.

The solution lies in preventing the process of stone evolution in the body by dealing with the chemical, pathological and especially the mechanical factors in the biliary system, which are involved in stone formation.

Septic stones.—It is the pathology of these which renders the gallbladder such an important organ in diseased conditions. From the point of view of treatment it is important to understand their method of formation. It is true that chronic cholecystitis frequently leads to stone formation, just as stone formation leads to inflammation. The chronic infection itself is only a secondary factor in stone formation, the fundamental issue in stone formation being obstruction to the outward flow of bile from the gallbladder. If only infection with inflammation were present, the products of that inflammation—mucus or pus—would depend on whether the infection is mild or severe; normal drainage would ameliorate the trouble, and the gallbladder would become healthy. But should the outward flow of the inflammatory products be interfered with, obstruction would lead to a damming back of the contents of the gallbladder, followed by precipitation of the solid constituents. If relief of the obstruction is brought about in a short time, these precipitated contents will still pass out; but if the time of obstruction is prolonged, solidification will occur, and harder masses will form, fresh layers being

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- Manson-Bahr, P. (1932). The Therapeutic Effects of Plasmoquine in Pregnancy. *Lancet*, Vol. I, p. 882.
 Napier, L. E., Butcher, D., and Das Gupta, C. R. (1932). Field Experiments with Atebrin and Plasmochin. *Indian Med. Gaz.*, Vol. LXVII, p. 186.
 Napier, L. E., and Das Gupta, B. M. (1932). Atebrin: A Synthetic Drug for the Treatment of Malaria. *Ibid.*, p. 181.
 Thakkar, K. V. (1929). Plasmoquine in Pregnancy. *Ibid.*, Vol. LXIV, p. 198.

deposited on these concretions with each attack of obstruction. When the mass is too large to escape by the natural outlet, it assumes a more important rôle; it becomes impacted in Hartman's pouch. Recurring attacks of acute cholecystitis occur with accompanying complications, such as perforation of the bladder leading to peritonitis, abscess formation, or, in chronic cases, to a contracted bladder, its dense adhesions causing reflex symptoms in the stomach, attacks of colic, jaundice, etc. Hence it is clear that the most predominant feature of gallbladder disease is obstruction, any co-existing infection being secondary; therefore removal of the obstruction should be the chief aim in treatment, though this may not be complete, for there may still be obstruction in the ducts. The main trouble with stones is their relation to the ducts, yet the basis of the operation of cholecystectomy is to give most attention to the bladder, thus ignoring the condition of the rest of the biliary passages which is the most vital factor in stone pathology; and it omits consideration of the 'pressure-gauge' function of the bladder, regulating back pressure on the liver, and the pancreas. Instead of relieving the block, removal of the bladder further increases the internal pressure on the tracts. Though after effects may be mild, they often become severe, as in chronic dyspepsia, or there may be chronic, or even acute, pancreatitis because the regulator of internal pressure has been removed. After cholecystectomy if these mishaps are avoided, there may occur an obstruction in the common bile duct due to other causes, such as the pressure of enlarged glands around the ducts, cancer, and adhesions, and the patient may be incurably jaundiced because, with the bladder removed, no further surgical assistance is possible.

It is true that in the hands of the expert the mortality from cholecystectomy has been lower than from external drainage, the former being 1.3 per cent, the latter 1.5 per cent. Drainage, however, is resorted to only in the more severe cases. There is no doubt that drainage is by far the easier and safer procedure in very severe cases, and it is safer still when the disease is limited to the gallbladder or is of mild degree. In such cases, internal drainage would be of more advantage to the patient, so that when the disease is limited to the bladder and is mild, internal drainage might well be performed. If, however, the patient's condition will not justify a prolonged anæsthetic, simple external temporary drainage can be carried out in the first instance as in acute obstruction, followed later, if the condition permits, by internal anastomosis.

Surgical factors.—Some of the difficulties which may be encountered in the surgery of this condition are: obscuration of the operator's vision of the area by hæmorrhage, and especially the difficulty of obtaining a good view of the

hepatic artery and portal vein, the difficulties of dissection of dense adhesions around the neck of the bladder, and sometimes the impossibility of completing the removal of the contracted bladder from among the adhesions. Finally there is the even more frequent risk of a permanent fistula after the operation.

It is therefore considered that neither cholecystectomy nor the milder cholecystotomy is the operation of choice in gallstone disease. Dependent and internal drainage of the obstructed biliary and pancreatic passages must be carried out, no matter how advanced is the disease.

The loss of the function performed by the gallbladder because of its removal is an important matter, for it will naturally have certain effects on the biliary and pancreatic ducts. In health, the flow of bile is continuous from the liver to the gallbladder and it varies but little with the intake of food. The bladder receives all the bile as it is produced until the reflex from the duodenum causes relaxation of the sphincter of Oddi and allows it to flow into the gut. The presence of food in the alimentary tract causes this reflex, and when there is no food there is a damming back of both biliary and pancreatic secretions with resulting back pressure on these two organs, and this is sure to influence health, causing secondary changes such as cholangitis or pancreatitis.

After cholecystectomy there may occur such complications as biliary external fistula, intermittent or progressive jaundice because of stones having been overlooked at the operation, or having reformed in the biliary tract, or there may be stricture or kinking of the common bile duct, owing to fibrosis. There are also grave dangers associated with anatomical variations in the bladder and its surroundings. Flint says that in 65 per cent of cases there are abnormalities of the cystic duct and cystic artery, and often, therefore, the operator has difficulty from this cause.

Dependent drainage by means of cholecystenterostomy is advocated because of the following considerations:

Ætiological.—Aseptic stones are formed in the gallbladder and in the biliary radicles, and when they are retained long they increase in size, being steeped in concentrated bile which contains a high cholesterol and bilirubin content, maintained by the abnormal metabolism of the body. By removal of the gallbladder, the formation of stones within it would be eliminated of course, but formation in the ducts would not be affected. If the concentrated bile were drained efficiently from the gallbladder and from the ducts, this tendency to long retention would be frustrated; and since we know of no means of regulating the normal metabolism of cholesterol, etc., we could at least prevent stone recurrence by removing stagnation of bile before crystallization could

take place. Removal of the bladder constitutes no remedy for stone disease, at least in the case of aseptic stones. By dependent drainage of the bile from the whole biliary tract, its constant removal can be assured, and small stones which have been overlooked will be included in the downward drainage. Moreover, if a stone forms in the hepatic radicles it will follow one of the two courses indicated below. If a stone passes straight into the common bile duct, it may enter the duodenum, and even temporary impaction will produce no worse result than colic, and the portion of the biliary system above the obstruction would be efficiently drained, seeing there is an additional bypass, and the part below the obstruction would drain naturally. If the impaction occurs below the union of the pancreatic duct with the bile duct, there will be no evil consequences, for the whole biliary and pancreatic system will be drained into the intestinal tract.

Septic stones are a result of infection plus obstruction, and removal of the latter does away with the cause of septic stone formation. Dependent drainage and anastomosis secure this. Septic stones form primarily in the gallbladder, and are due to obstruction to the outlet at its neck, at the cystic duct by either stone impaction at Hartman's pouch or in the cystic duct by contraction, growth, or the swelling of the cystic duct. The ease with which the cystic duct may be obstructed is not surprising, as its lumen is not more than one-eighth of an inch in diameter. With efficient drainage at the base of the bladder it is difficult to see how stagnation or sedimentation can take place for long. But even if a small stone were formed, it could pass more comfortably through the larger aperture in obedience to gravity. The idea that cholecystitis leads to secondary stone formation in the gallbladder is countered by the fact that no septic nucleus would remain long enough to acquire the solidity or size necessary to render it pathological.

If a stone forms higher in the liver ducts, it will slip towards the more open duct lower down. After anastomosis, there is a choice of two courses for the stone; it may become impacted anywhere along the common duct, the position depending on other factors, and a similar course would be followed by any stone recurring and forming in the common bile duct. If firmly impacted it will block the natural path higher up, but with no adverse results, for the bile would be diverted along the artificial channel, and the pancreatic secretions will follow the normal course through the ampulla of Vater if the impaction is above the duct junction. Neither will there be any bad consequence if the impaction occurs at the ampulla, as the pancreatic secretions can flow along the alternative path, through the bladder into the duodenum.

Hence it is clear that cholecystenterostomy is not only a treatment for the stone disease present when a patient is operated upon, but is also a prophylactic measure against stone recurrence; the surgical treatment of any biliary condition is in my opinion not removal of the portion at fault, but effective drainage.

Pathological and mechanical factors.—The shape of the bladder, tapering as it does from Hartman's pouch towards the spirally coiled cystic duct only one-eighth of an inch in calibre, the common bile duct which is long and flaccid and passes among numerous glands so it is often pressed upon by them, the defective propulsive power from the gallbladder, and the very dependent position of the gallbladder fundus, which is aggravated in man's erect posture, are all against a satisfactory natural emptying of the organ, and so there are endless possibilities of obstruction. If the danger of recurrences mentioned above could be removed, gone would also be the nightmare of cancer formation.

Advantages of cholecystenterostomy.—If at the time of operation any irremovable obstruction were present, it would not be necessary to hazard a difficult dissection among dense adhesions, nor even an incision into the common bile duct in order to extract an impacted stone. The procedure advocated would be a safeguard against any future stricture obstruction. Even if the stone in the common duct were firmly impacted and irremovable, it would cause no harm, as it would be enveloped by fibrosis at the site of impaction, and the bile would pass through the artificial passage. Anastomosis could even be substituted for the difficult removal of a firmly impacted stone requiring retroduodenal interference. The same operation by a modified technique to be mentioned, is applicable to a contracted gallbladder where external drainage might be done. It also meets the risk connected with an irremovable fibrosed gallbladder which is a great source of focal infection and irritation tending towards cancer formation. It needs no dissection round the neck of the bladder, there is no danger to surrounding structures, and it is safer, easier, and freer from complications than other methods of operative interference.

Surgical and anatomical factors.—The gallbladder lies beneath the liver, with its most dependent part in contact with the first and second parts of the duodenum; it tapers to a fine spiral tube pointing upwards and backwards, which joins the common bile duct; thus the evacuation of bile is considerably hampered by gravity, and this is further aggravated by the valve-like effect of Hartman's pouch. Poor as it is under normal conditions, the exit of biliary contents is rendered more difficult when the bladder is diseased. In acute cholecystitis the predominant feature is obstruction, for without that no serious harm would follow.

Here again an emergency exit at the fundus is easily made under local anæsthesia, and will solve the difficulty; thus cholecystenterostomy in two stages can be applied to the relief of the acute disease with benefit equal to that already stated in relation to less acute forms.

The cholecystitis may be a primary affection leading to stone formation. There may be a chronic inflammation in the bladder walls, causing ill-health through septic absorption, or it may result in stone formation. There is a constant tonic effect on the bladder walls, which is aggravated by the chronically inflamed mucous membrane, and the walls remain in persistent spasm, as shown by the reflex pain at the bladder point on the abdominal surface.

With man in the erect posture, the cystic duct is already at a disadvantage in the matter of natural drainage, and in recumbency this is aggravated by the kinking of its walls caused by the weight of the bladder contents. A dependent bypass at the fundus will act as a gravity outlet for any stones would otherwise pass along the natural path.

The advantages of this operation are enhanced by its safety and simplicity, and by the elimination of the danger of damage to structures around the neck of the gallbladder. Any impacted stone which is present can be aspirated, spooned up, or milked up, as it will pass more easily back towards the dilated part of the duct above. If removal of the stone is not possible in this way, incision into the common bile duct over the site of impaction, and subsequent transverse suture can be performed. With a shrunken and fibrous gallbladder, buried in deep adhesions, drainage internally is easier and safer. In a difficult case with a small bladder the operation is best carried out in two stages. Cholecystenterostomy is also indicated in stone impaction in the common bile duct, partly as a cure of the condition, and partly as a precaution against stricture.

Simple external drainage often means fistula formation, with loss of bile, so that the patient must tolerate oral feeding with bile for the rest of his life. But if the external fistula were closed, it might mean a shorter and an inefficient drainage, leading to blockage and the aggravating factor of focal infection, which the external drainage might have temporarily relieved, and which had been ignored at the previous operation. If there is an internal fistula, the drainage after this operation would be most efficient and permanent. It is much easier than a reconstruction of the passages such as would be required in external drainage; also the focal infection could be permanently relieved.

THE CHOICE OF OPERATION IN DEPENDENT DRAINAGE OF GALLBLADDER

The relationship of the gallbladder to the pyloric end of the stomach, the first and second parts of the duodenum, the jejunum and the

colon renders anastomosis of the organ with one of them quite easy. The duodenum is not difficult to appose when there are no dense adhesions. The choice of the site of anastomosis of the gallbladder to the alimentary tract depends upon the advantages to the patient from the standpoint of safety and ultimate benefit.

With regard to anastomosis with the stomach, the part of that organ to consider is that lying in close apposition to the gallbladder, that is, the anterior surface towards the lesser curvature, near the pyloric end, just proximal to the pyloric vein, about one and a half inches from the sphincter of the pylorus. The main drawback in this anastomosis is that the alkaline biliary secretions tend to neutralize the acid gastric secretions, thus interfering with digestion in the stomach, and so inducing dyspeptic complications with biliary vomiting. But when the gastric acidity is abnormally high, as in the hypermotile stomach, this objection is not so important. The rarity of a secondary ulcer at the site of the anastomosis in gastroduodenostomy is due to the bile projected so near that site. The choice of the anastomosis of the gallbladder with the stomach should be based on a preliminary investigation of the gastric contents, the estimation of acidity, and radiological observations to ascertain the activity of the organ.

Where gastric analysis shows a low acidity of gastric contents, and the radiogram reveals a large dilated stomach, the ordinary treatment for gastric ulcer would be a posterior gastro-jejunostomy, even if there were associated gallbladder disease. Here recurrence of the ulcer would not be likely, and the existing gastric ulcer would heal, for the pathological condition is obstruction in the stomach, rather than acidity. Biliary anastomosis is not likely to be of assistance and some other site for apposition would have to be chosen. Where gastric acidity is low, with a dilated stomach, a gastro-jejunostomy would ordinarily be performed for an associated gastric ulcer and the gallbladder in such a case would not be apposed to the stomach. Anastomosis with the colon would lead to the digestive process being deprived of the bile, and would produce irritation of the colon causing frequent motions, as well as the great danger of infecting the biliary tract from the colonic contents. Anastomosis with the jejunum entails drawing up a loop of the small intestine in front of the duodenum and the stomach, thus introducing the troubles of kinking, torsion and looping of the jejunum, with obstruction. Also it diverts the bile too far down, thus increasing the liability to duodenal ulcer. Should a later operation be necessary for a gastric ulcer, a posterior gastro-enterostomy would be dangerous, on account of the great liability to post-operative obstruction. Hence the jejunum is not a suitable site for

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CHRONIC AMŒBIC INFECTION AS A CAUSE OF ILL-HEALTH

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It is impossible to practise for any length of time in this portion of the tropics without being struck by the number of patients suffering from general ill-health the cause of whose trouble has not been diagnosed. These patients drift from doctor to doctor, from one consultant to another, and in and out of hospital. In default of relief they provide a fruitful field for homœopaths, nature healers, compounders, indigenous practitioners, and quacks of all sorts, and they certainly do not add to the repute of western medicine. In many of them, owing to the combination of low fever, loss of weight and appetite, and, frequently, abdominal pain or discomfort, with or without diarrhœa, the diagnosis of tuberculosis is made, with its resultant load of anxiety and useless treatment; in others, often rightly, the condition is attributed to the degree of pyorrhœa present, which is so often found in Indians.

It is my object, in this note, to call attention to the third member of this triad—chronic infection with *Entamoeba histolytica*, or amœbiasis. With cases of frank dysentery, in its clinical sense, I shall not deal. Apart from the recognition of the infection by the character of the stools, the entamoeba is usually readily found. It is with cases of chronic infection that I am concerned.

A history of precedent dysentery, and, still more often, the absence of such history, I have found to be of very little value in diagnosis. Patients are forgetful; bowel derangements are common in India; the significance of 'dysentery' in the layman's mind is so varied. Even early attacks of amœbic dysentery may be characterized by diarrhœa only, without the obvious mucus and blood which leads to the label of

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gallbladder anastomosis. With regard to anastomosis with the duodenum, this is the next easiest part with which to join the gallbladder. Surgically there may be difficulty in mobilizing the duodenum, but this is overcome by an incision parallel to its right side along the line of fusion of the four layers of the peritoneum covering the organ. Where there is difficulty owing to a contracted gallbladder, a T-shaped tube, with one limb in the bladder and the other in the duodenum, forms a temporary external drainage which later can be allowed to close while internal drainage continues. In a person with a normal stomach, anastomosis with the duodenum should be given preference, as it is more allied to the natural cure of the gallstone disease.

'dysentery'; therefore little reliance can be placed upon any but the most definitely positive history as suggesting the presence or absence of this infection.

Rogers (*Tropical Medicine*—Rogers and Megaw) gives, as indications of amœbic disease, a history of repeated relapses, thickening of the cæcum and ascending colon, tenderness due to local peritonitis, and hepatitis or enlargement of the liver. In the cases I am quoting below these points are well brought out and, in addition, I hope to be able to demonstrate that many cases of this infection fail to show even these signs, and some only suffer from general ill-health.

I have divided the cases into four groups:—

1. Cases with definite abdominal derangement, with signs of the involvement of upper colon or liver.

(a) Proved microscopically.

(b) Unproved.

2. Cases with abdominal symptoms, but with no definite objective signs.

3. Cases of general ill-health, without abdominal localization.

4. Cases under treatment for some other disease, found to be infected with *E. histolytica*.

The notes are abbreviated as much as possible.

Group 1.—These cases have the most definite symptoms, and should mostly be easily recognized. The first four were proved; in the other six the amœba could not be demonstrated, but it will be seen that their symptoms were in no way less suggestive than those of the others. Cases 9 and 10 had signs of liver involvement.

Case 1.—Hindu male. Previously treated in hospitals in America for 'ulcerative colitis'. For over a year suffering from attacks of looseness of stools with occasional blood and mucus, from almost constant discomfort and pain below the umbilicus, excessive weakness, and evening fever, latterly up to 101°F. Nothing objective found except general abdominal resistance and epigastric tenderness. In the third stool examined active *E. histolytica* were found. Thorough treatment by emetine resulted in disappearance of 'dysentery', fall of temperature, and general improvement.

Case 2.—Hindu male, aged 34, complains over a period of five months of fever, constipation, and right iliac pain. Previously diagnosed as pulmonary and also as abdominal tuberculosis, and treated by calcium and other therapy. Tender, gurgling, palpable cæcum, no enlargement of liver, no lung signs, fever to 99.5°F. daily. Sputum negative for tubercle bacilli, Wassermann reaction negative. Stools showed constant presence of cysts of *E. histolytica*. Treatment by emetine hydrochloride intramuscularly and emetine bismuth iodide orally resulted in disappearance of fever and much remission of symptoms.

Case 3.—Mohammedan female, aged 30. Chronic abdominal discomfort for six months with low fever for 3 months, and loss of weight. Was sent to hospital as a case of abdominal tuberculosis. Thickened gurgling cæcum, liver normal, stools showing dead amœbæ on each of three occasions. Treatment by emetine injections and emetine bismuth iodide produced considerable improvement, and fever settling down and pain being much relieved.

Case 4.—Hindu female. Chronic pain for one year in abdomen, especially right iliac fossa, occasional fever, chronic constipation, and loss of weight and

appetite. Abdomen soft and flabby with thickened and flatulent cæcum. Stools showed dead amœbæ. Treatment by emetine produced gradual but steady relief.

Case 5.—Mohammedan male, aged 19. Constipation for two years, constant abdominal discomfort for one year, attacks of frequent watery motions for four days (40 to 50 per day). Thickened cæcum present and right iliac tenderness. Stool examination repeatedly negative. Emetine hydrochloride, nine grains in one grain doses, was given before patient left hospital on account of relief of symptoms.

Case 6.—Hindu male, aged 24. Right lumbar pain of five years' duration, dull in character, lasting six or seven days at a time, loss of weight, appetite and strength. Previously diagnosed as abdominal tuberculosis and treated by twenty injections of tuberculin and twelve of Jacobsen's fluid, without result. No physical signs whatever except for a thickened cæcum, gurgling and tender on pressure. Stools negative. Emetine therapy was commenced, but patient left hospital too early for any result to be noted.

Case 7.—Hindu male, aged 23. For two years attacks of fever, alternating constipation and diarrhœa, loss of appetite and pain in right iliac, right hypochondriac, and umbilical regions. A thickened tender cæcum was found on palpation. Stool examinations negative. Treatment by emetine resulted in relief of symptoms.

Case 8.—Sikh male. Frequent attacks of diarrhœa over a period of six months, lasting two or three days, and recurring every fortnight or so. Suspected of being tuberculous. Stools yellowish with mucus at times but no blood. General abdominal discomfort with loss of appetite. Definitely thickened and tender cæcum, tenderness in right hypochondrium, and a palpable liver on deep breathing. Repeated stool examinations negative. On clinical diagnosis emetine treatment was instituted, and improvement was marked.

Case 9.—Hindu male, aged 30. Fever starting four months before, with enlarged and painful liver. Liver said to have been punctured and 'a bead of pus' obtained. He was treated with emetine. Anæmia, puffiness of face, liver enlarged to within 1 inch of umbilicus, and a localized œdema of the epigastric wall; slight ascites and right basal pulmonary crepitations. Stools loose and yellow, no mucus, two to three daily; repeated examinations failed to show amœbæ or cysts. Total white cell count 20,160 with 88 per cent polymorphonuclears. Treatment by emetine and emetine bismuth iodide, followed by anabin, produced a gradual but steady improvement, with diminution in size of liver and fall of white cell count to 8,000.

Case 10.—Hindu male. Fever for two months, accompanied by enlargement of liver, following an attack of 'clinical' dysentery three months back. The liver, which was enlarged by four finger-breadths, was firmer than is usually found in amœbic hepatitis. Total white cell count 12,080. No amœbæ or cysts were found in the stools. Wassermann reaction negative. Treatment by emetine was started, the fever subsided and the liver became less, but after eleven grains were given the patient left hospital.

Group 2.—These cases present definite abdominal symptoms but no physical signs. They varied in degree from frequently recurring dysentery to simple abdominal derangement with or without diarrhœa. In all save one microscopic examination of the stools gave a positive result.

Case 11.—Hindu female, aged 50. Attacks of frequency of stools, with passage of blood and mucus, and griping pain, over a period of one year. Physical examination negative except for tenderness on deep pressure in right hypochondrium. Stools loose containing blood and mucus and a few active *E. histolytica*. Treatment by emetine led to marked improvement.

Case 12.—Hindu female, aged 28. Diarrhœa for eight months, with abdominal pain and bouts of fever. Legs œdematous; debility and emaciation extreme. No local abdominal signs. Stools containing mucus and active

E. histolytica. Failed to react to treatment and died after three weeks.

Case 13.—Mohammedan male, aged 35. For six years almost weekly attacks of loose stools followed by constipation, with slight abdominal pain and much flatulence. During the hot season attacks are almost continuous. Only previous history 'typhoid fever' in 1924. Tenderness in umbilical and right iliac regions, but no thickening of the cæcum, and spleen and liver not palpable. Stools negative. On a clinical diagnosis of chronic amœbiasis he was given twelve grains emetine hydrochloride and left hospital much improved.

Case 14.—Hindu male, aged 30. Attacks of colic for two months and fever for one month. No physical signs except resistance and tenderness over gallbladder. No increase of blood cholesterol; no leucocytosis; polymorphonuclears 80 per cent. Visualization showed a long pendulous gallbladder but no stones. Stools showed large numbers of cysts of *E. histolytica*, *E. coli*, and a few of *I. butschlii*. Treatment by emetine hydrochloride and emetine bismuth iodide caused disappearance of cysts and subsidence of fever. He has remained well since.

Case 15.—Indian-Christian female, aged 24. Long-continued vague abdominal pain and discomfort and irregularity of bowels; slight fever for six weeks past; suspected of suffering from tuberculosis. Physical examination negative. Stools regular in time and character. Examination after administration of sodium sulphate showed first dead amœbæ and cysts, and subsequently active *E. histolytica*. Emetine treatment produced relief. The patient also suffered from attacks of lumbar pain, and radiologically the presence of a ureteral calculus was shown.

Case 16.—Mohammedan male, aged 20. Chronic constipation over a period of four years, with abdominal discomfort and loss of appetite, and recent fever with cough and cold. Two years previously found to be harbouring ankylostomes, *Hymenolepis nana* and *E. histolytica*, and had been treated with emetine. Thought he was suffering from tuberculosis. No physical signs in chest or abdomen. Stools contain a fair number of *E. histolytica* cysts and other protozoal parasites. Treatment by emetine and other amœbicidal drugs, over a period of a month and on a second admission three months later, when cysts were still found, produced considerable improvement.

Case 17.—Hindu male, aged 24. Constipation and loss of weight over a period of ten months. Cysts of *E. histolytica* had been found nine months before admission, and seven grains of emetine hydrochloride were given without result. No physical signs on examination. Stools, after several attempts, showed cysts of *E. histolytica*. Relief followed treatment.

Group 3.—The third group comprises cases where little is complained of except general ill-health, usually with fever of chronic type. These cases have often been diagnosed as tuberculosis, and there is little to suggest at first sight that they may be suffering from amœbiasis. Case 20 declared himself while in hospital by developing an acute attack.

Case 18.—Hindu male. Came to hospital suspected of pulmonary tuberculosis, suffering from fever for four months and loss of appetite and weight. Lung examinations, both clinical and radiographic, were negative. Wassermann reaction negative. No glandular enlargements. No physical signs. Stool examination showed active *E. histolytica*. There was no history of dysentery. Treatment by emetine produced relief of symptoms, the fever subsiding after the sixth injection.

Case 19.—Hindu male, aged 46. Admitted for fever up to 102°F. and cough lasting two months, and general weakness. Hæmoptysis of chocolate-coloured material for a few days a month before admission, and once later bright blood. No objective physical signs. One small specimen of blood expectorated suggested liver abscess material. Total white cell count only 8,800; liver not enlarged. Radiogram of chest showed calcified

glands only. Sputum and stools negative. Emetine and other amoebicidal drugs led to relief of symptoms and fall of fever. During injections he once complained of pain in the liver, and had a slight hæmoptysis, and on one occasion had diarrhoea.

Case 20.—Hindu male, aged 40. Loss of appetite and slight fever for over four months, and loss of weight and anæmia. Suggestion of tuberculosis. No physical signs found except severe anæmia with total red cells 3,500,000 and a blood picture of secondary anæmia. In hospital developed dysenteric motions containing large numbers of *E. histolytica*. In spite of stimulant and anti-amoebic treatment his condition gradually became worse and he died after seven weeks.

Case 21.—Anglo-Indian female. Admitted for low fever and loss of appetite; no other symptoms whatever. Lungs clear clinically and radiographically. Total white cell count 11,000 with normal differential count; night and day blood negative; urine sterile. No abdominal or bowel symptoms, but examination of stools showed active *E. histolytica*. Treatment by emetine led to subsidence of fever, and gradual improvement of health, with increase of weight.

Case 22.—Mohammedan male, aged 35. Low evening fever and loss of weight over three months. A year before had been operated on for fistula in ano. The suggestion was that he was suffering from tuberculosis, but there was no history of cough or hæmoptysis, nor of dysentery or any abdominal complaint, and there were no physical signs, abdominal or pulmonary. Stool examination showed active *E. histolytica*. Treatment by emetine was bringing some relief when patient left hospital for private reasons.

Group 4.—This case illustrates the finding of *E. histolytica* in a patient under treatment for another complaint. In a country like India, where multiple infections are common, such a possibility must never be lost sight of.

Case 23.—Hindu male, aged 24. In hospital for treatment of hookworm infection with severe anæmia. After several treatments with thymol and removal of a number of ankylostomes he developed dysenteric motions, found to contain active *E. histolytica*. Treatment by emetine injections and subsequent emetine bismuth iodide produced rapid relief.

With the above cases I hope to have illustrated the prevalence of chronic amoebiasis even where it may not be at once suspected. The importance of realizing this fact I need not emphasize. Many of these patients believe themselves to be suffering from tuberculosis, usually of the abdominal type, and it is very common indeed to find that they have undergone various treatments directed against that infection. To rescue even a proportion from the mental worry, useless expense, and waste of time involved is itself an achievement.

It is not only practitioners in the tropics who have thus to be on their guard: those who are practising in temperate regions to which patients from the tropics retire or go on leave may also be confronted with the same problem, though their main interest lies in the fact that the symptoms complained of by these sufferers suggest the diagnosis, not infrequently, of appendicitis, and Rogers (*Recent Advances in Tropical Medicine*) points out the frequency with which chronic dysentery patients appearing before the Medical Board of the India Office have had their appendices removed without any permanent benefit.

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BRONCHOSCOPY : ITS USEFULNESS IN INDIA

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BRONCHOSCOPY is the art of examining the trachea and bronchial tree by looking through a rigid tube which serves as a speculum. Laryngoscopy and œsophagoscopy are terms which are applied to the similar examination of the larynx and œsophagus, respectively. These procedures collectively are commonly included in the general term 'bronchoscopy'.

This specialty has been mainly built up during the past twenty-eight years by Dr. Chevalier Jackson and his associates in Philadelphia. At first bronchoscopy was used principally for the removal of foreign bodies from the air and food passages, and sometimes the results were very spectacular. One operation requiring the utmost skill was the removal of four safety pins from the œsophagus of a small child. These safety pins were open and interlocked and the points of all were pointing upward. The great variety of foreign bodies removed includes coins, buttons, tacks of various kinds, bone or bone fragments, beans and other kinds of seeds, dry cell (battery) caps, dentures, needles and various kinds of pins, in fact almost anything that an adult or child is likely to put into the mouth.

At present, however, the foreign body cases constitute less than 2 per cent of all the cases in the Philadelphia bronchoscopic clinics. This is not because foreign body cases are fewer. They are indeed more numerous, but the field of bronchoscopy has so greatly widened. Some of the other uses of bronchoscopy are: aspiration of lung abscesses, aspiration of bronchiectatic cavities, cure of 'post-operative pneumonia', which is really atelectasis caused by the obstruction of a bronchus by tenacious mucus, diagnosis of lung tumours, early diagnosis and treatment of cancer and other tumours of the larynx or œsophagus, diagnosis and treatment of stricture and ulcer of the œsophagus, as well as the diagnosis and treatment of cardiospasm, 'lung mapping', by injecting

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I have come to look upon the presence of right iliac symptoms, much short of signs such as Rogers cites, as suggestions of chronic amoebiasis even in the complete absence of clinical dysentery or of diarrhoea. Many of these patients, far from complaining of looseness of the bowels, emphasize the presence and frequency of constipation and may have attributed any diarrhoea to purgatives they have taken in consequence.

I am indebted to Dr. P. N. Wahi, my late house physician, for most of the case notes. The pathological examinations were carried out in the pathology department of King George's Medical College.

lipiodol through the bronchoscope into the exact portion of the lung where it is wanted and then taking an x-ray plate to visualize the extent of the lesion. This last procedure is especially valuable before attempting the more radical operations of thoracic surgery such as thoracoplasty and lobectomy.

The technique of performing a bronchoscopy is briefly as follows:—The patient lies on the operating table in the dorsal position, the head and shoulders being supported by the first assistant who sits at the patient's right. The first assistant holds the head in such a manner that the neck is sharply flexed at the seventh cervical vertebra and sharply extended at the occipito-atloid joint. He also keeps the mouth open by means of a special mouth gag or 'bite-block'. A second assistant keeps the shoulders well down on a level with the table. With the patient in such a position the operator can insert the laryngoscopic speculum or laryngoscope, lift the epiglottis forward and obtain a direct view of the larynx and vocal cords. He then passes the tubular bronchoscope through the laryngoscope and insinuates it between the vocal cords and well into the trachea. The heavy laryngoscope is then removed and the bronchial tree is leisurely and thoroughly explored, the patient breathing through and around the bronchoscope. The direction of the bronchoscope can be varied at will by directing the first assistant to change the direction of the head of the patient. When a foreign body is encountered, a long and very delicate forceps is passed through the bronchoscope and the foreign body is grasped while in view of the operator, and removed. In the early days bronchoscopy was attended with considerable mortality. But now the development of technique and team work, together with the elimination of general anaesthesia, have practically done away with deaths.

General anaesthesia is never used in the Chevalier Jackson bronchoscopic clinics. No anaesthesia whatever is given to children under 10 years of age. For bronchoscopies in adults 4 per cent cocaine is applied to the pyriform sinuses and 1 c.cm. of 4 per cent cocaine is advantageously injected intratracheally. For oesophagoscopies 10-15 drops of cocaine hydrochloride 4 per cent solution are placed on the base of the tongue and swallowed. For bronchoscopies in adults a preliminary hypodermic of morphine sulphate $\frac{1}{4}$ to $\frac{3}{8}$ grain and 1/150 grain of scopolamine is given one hour before the patient goes to the operating room. No food or water is given for five hours prior to any endoscopic procedure. Rectal anaesthesia may advantageously be given in the case of very nervous and apprehensive patients.

It recently has been my privilege, after taking Dr. Jackson's personal course in bronchoscopy, to serve for three months as an assistant both to Dr. Chevalier Jackson and to Dr. Louis H. Clerf. During that time it was my good fortune

to perform 103 bronchoscopies and 5 oesophagoscopies.

Since returning to Vengurla from furlough there have been a rather limited number of bronchoscopic procedures, 14 in all. There have been no mortalities. The patients are usually up and about on the same day, or the day following the procedure. Three cases are reported as follows:—

Case 1.—A case where oesophagoscopy was of distinct advantage was that of J. D. M., male, 52 years old, emaciated, who, for seven months, had vomited all solid food five minutes after swallowing it. Liquids were swallowed very slowly and with increasing difficulty. X-ray examination showed an obstruction in the lower third of the oesophagus with considerable dilatation above the stricture. The oesophagoscope disclosed a constriction about 16 inches from the teeth with an irregular gray, nodular object the size of a pea fitting into the constriction and evidently acting like a ball-valve in retarding the passage of food. It was evidently made up of decomposed and adherent food particles for when removed it broke up like a dried blood clot. Also at the constriction, a small sub-epithelial tumour-like body protruded into the lumen and evidently aided in the valve action. The oesophagoscope was passed beyond the constriction however, and into the stomach.

The ordinary oesophageal bougies were passed after several days but met with an obstruction about 16 inches from the teeth. Had they been forced down they might have perforated the oesophagus and caused a fatal mediastinitis. However the patient was directed to swallow, slowly, a strong linen thread 15 feet long. On the end of this was threaded the perforated olive tip of a hydrostatic oesophageal dilator. With the thread as a guide the tip of the dilator readily passed the obstruction and then was inflated to 10 pounds pressure for 5 minutes.

Thereafter the patient was encouraged to take, gradually, solid food and he left the hospital eight pounds heavier, an exceedingly grateful patient. He denied syphilis and his Kahn test was only + +, yet we pushed anti-leucic therapy and believe this to have been a case of gumma of the oesophagus. Had it not been for the oesophagoscope, he probably would have suffered the misery of gastrostomy.

Case 2.—R. R., a weak old man of 58 years with terrible dyspnoea, was admitted on 10th November, 1931. He stated that he had had difficulty in breathing since an operation on the right nostril one year ago. The right nostril was stenosed and on auscultation over the chest a flapping sound was heard at the beginning of each wheezing inspiration. Mirror laryngoscopy revealed a paralysed epiglottis which flapped down over the entrance to the larynx and almost prohibited the entrance of air.

A similar picture, though inverted, was seen by direct vision, using the Jackson laryngoscope. Through this tubular instrument was passed the laryngeal cup forceps, and the epiglottis was partially amputated by cutting off its edge. By this procedure the dyspnoea was lessened, but when the epiglottis was raised upward it was seen that the entire larynx was in a softened paralysed state so that on each inspiration its walls and the inter-arytenoid tissue collapsed, closing the lumen almost completely. The unfortunate old man refused tracheotomy and continued to breathe laboriously for several days; then he became unconscious from respiratory collapse. He stopped breathing on the operating table while tracheotomy was being performed and was revived with difficulty. He gained strength rapidly however and was a most grateful patient when he left the hospital on 16th March, 1932, wearing his tracheotomy tube.

Case 3.—S. D. S., a young woman of 19 years, had hæmoptysis, occasional and slight, for nine months

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FÆCAL BACTERIA IN BENGAL AS INDICATORS OF SEWAGE CONTAMINATION OF WATER: A PRELIMINARY STUDY

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and

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(Read at the Indian Science Congress, 1933)

THE method which we follow in the bacteriological analysis of water in Bengal was based on that used by Col. Clemesha in the study of flora of the human faeces in Madras. As the diet of the people of the Presidency of Bengal differs somewhat from that of the people of Madras, one might suspect the faecal flora of the two provinces to be not quite the same. A detailed bacteriological examination of the stools of this province may prove to be of help in assaying the import of these bacilli, individually and in association, in interpretation of the result of analysis of water, so we have examined the stools of twenty-five persons of this province as a preliminary measure.

Colon bacilli in Bengal faeces:—In his research in Madras, Col. Clemesha examined 751 colonies of lactose fermenters from forty-three stools; we examined 734 colonies. They were identified by the fermentation tests on saccharose, dulcitate and adonite, by the alkali-red reaction of Voges and Proskauer and by the indol reaction; to these we added the citrate utilization test of Koser. They of course all fermented lactose with production of gas, that is, were members of the *Bacterium coli* group. The different species of *bacterium* found in these stools are shown in the table on the next page.

(1) *Species of bacterium*.—Clemesha found 22 different bacilli in Madras, we also found 22 in the Bengal stools examined.

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preceding admission to this hospital. She had been treated in a sanatorium with some relief, but had had several small hæmorrhages during the month before she came to us. There was slight cough but no fever. There were five examinations of the sputum during her stay of three months in this hospital. All these examinations were negative for tubercle bacilli, but on two occasions spirilla were found. Frequent physical examinations of the lungs were uniformly negative. A bronchoscopy was done in the hope of finding a bleeding point. None was found and the bronchial mucous membrane appeared normal. Swabs were taken from the bronchial mucous membrane but no tubercle bacilli nor spirilla were found. However, after the bronchoscopy there were no more hæmorrhages. The patient was discharged apparently cured after twelve days and we believe that in case of a recurrence of hæmoptysis she would probably have returned to us, since she lives near by.

The cases to date have been comparatively few but, from their variety and from the results obtained, we feel that there is a distinct field of usefulness for bronchoscopy in India.

(a) Fourteen of these are common to the two provinces, viz, *Bact. coli commune*, *Bact. neapolitanum*, no. 101, *Bact. cosecoroba*, no. 75, *Bact. rhinoscleroma pneumoniae*, *Bact. vesiculosum*, *Bact. coli mutabile*, *Bact. lactis aerogenes*, *Bact. acidi lactici*, *Bact. cloacæ*, and the rarer ones *Bact. levans*, and nos. 33 and 67.

(b) Eight were present in the Bengal faeces but not in Madras, viz, nos. 111, 74, 104, 99, 36, *Bact. oxytocum* and nos. 97 and 66.

(c) Eight were absent in the Bengal faeces though found in Madras, viz, nos. 6, 9, 10, 37, 38, 39, 70 and 105.

(2) *Relative prevalence*.—In both the provinces, none of the species were present constantly in all the faeces. But while the striking feature in Madras was the continual steady presence of *B. vesiculosum* and *mutabile*, *B. cosecoroba* and to a less extent *B. coli commune*, in Bengal *B. neapolitanum* is decidedly at the top of the list, being present in 80 per cent of the stools and giving 17.8 per cent of the total number of colonies. This is followed by *B. coli commune*, *B. cosecoroba* and *B. vesiculosum*, the first of which was present in 72 and the other two each in 50 per cent of the faeces and they gave respectively 10.2, 9.6 and 9.5 per cent of the total colonies. Though giving about half these number of colonies or less, no. 101 was found in 64 per cent of the faeces, no. 75 and *B. lactis aerogenes* each in 48 per cent and *B. rhinoscleroma pneumoniae* and *B. acidi lactici* in 40 per cent.

Periodical variation, if present, cannot possibly be detected from examination of some 25 or even one hundred colonies from each stool, as it contains from 100 to 1,000 million colon bacilli and more per gramme, of at least 22 different kinds and perhaps others which were missed on account of the paucity of the number of colonies examined.

The members of class I of Clemesha in the Madras stools were *B. coli commune*, and nos. 39 and 70. In Bengal we also found *B. coli commune*. Besides this, the only other members of the class I found here were no. 36, *B. oxytocum*, *B. perniciosum* and no. 97; the first two were present only in 12 per cent of the faeces and the last one in 4 per cent. Taking these three together, the number of their colonies were about 4 per cent of the total.

Class II is represented in the Bengal flora by *B. neapolitanum*, no. 101, *B. cosecoroba*, *B. rhinoscleroma pneumoniae*, *B. lactis aerogenes*, *B. acidi lactici* and no. 33, the first eight in the table very liberally, being found in 40 to 80 per cent of the faeces and together giving about 50 per cent of the colonies.

Significance of these bacilli in water as indicators of recent sewage contamination:—

(a) In about 75 per cent of cases of recent sewage contamination of water, it appears from the above that we may expect the presence of *B. coli commune* and perhaps some of the other

TABLE

Species.	25-5-31		26-5-31		7-6-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3-32		1-3-32		15-3-32		2-12-31		9-8-31		9-8-31		12-7-31		1-8-31		1-4-32		19-3	
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three members of class I also. We found among the 25 colonies from one of the stools, two of the *B. oxytoca* as the only such indicator, there being none of the *B. coli commune* group among them. But in six of these stools, that is in 24 per cent, we had none of these class I bacilli. Thus if we take the presence of bacilli of class I as the test for recent pollution of water, 24 per cent of polluted water will pass this test.

(b) In the stools nos. 1 and 12 containing no bacilli of class I, *B. lactis aerogenes* with only one other member of the class II occurred in association with a larger number of species of class III. In the case of stool no. 1 the colonies of *B. lactis aerogenes* were only three and those of the other class II bacillus, *B. neapolitanum*, two out of the total number of 48 bacilli examined, while *B. no. 74* gave 17 and *B. cloacae*, 13. So if the water inoculated with this sewage were further diluted and only 10 colonies were examined, as is usual in practice, the only species found would have been *B. no. 74* and *B. cloacae* either without any bacillus of the class II or with only one or two colonies of these two classes. In the former case the bacilli would have been passed over in the case of surface waters, according to the Clemesha standard, and, in the latter case, the contamination would have been regarded as sufficiently advanced in purification to be passable for drinking. In the case of stool no. 12 the class II bacilli, *B. lactis aerogenes* and *B. acidi lactici* formed fourteen out of the 25 colonies; with dilution and examination of only 10 colonies, the contaminated water would also have been passed as of fair standard of purity. So with Bengal faeces even the criterion of mixture of bacilli of classes II and III may be misleading.

(c) As to the Koser's citrate utilization test developed since the days of Clemesha, in stool no. 1, 46 out of 48 colonies were citrate positive, the two exceptions being of *B. vesiculosus* two colonies of which utilized the citrate. All the 44 colonies of another stool not entered in the list acted on the citrate; and only one out of the 22 colonies of another such stool was citrate negative. Therefore, especially when we limit ourselves to only 10 colonies in our practical work, it may be quite possible to get only citrate utilizers in water recently polluted with human faeces.

Conclusion.—Absence of any colon bacilli in 60 c.cm. of water may show it to be free from sewage contamination and their absence in not less than 10 c.cm. may be a fair standard of purity for surface waters. But when they are present in any water in larger numbers, it is questionable, in face of the above facts, if such water can be passed for drinking, even if the class I members are absent or if a few of the class III ones are alone present or if a class II

one like *B. lactis aerogenes* predominates, associated perhaps with one or two other bacilli of these two classes. Clemesha had to relax the quantitative standards for surface waters because in his time few waters of the waterworks in Madras would pass them. The qualitative tests in question, relying on particular members of the colon groups or combinations of them as indicators of the pollution, were introduced by him as a necessary safeguard in such cases. Happily of late, bleaching-powder and other preparations are coming increasingly into use for final purification of the water, and appliances like chlorinators are making it easy to control the dose of the chlorine so as not to leave any of it to reach the consumers though it is sufficient to purify the water. Having regard to all these facts, may we not tighten the screw and insist on a higher standard of water purity on the quantitative basis?

REFERENCE

Clemesha, W. (1909). *A Study of the Bacteriology of Drinking Water Supplies in Tropical Climates*. (Being Appendix no. 1 to the Annual Report of the King Institute of Preventive Medicine, Madras, for 1905.) Madras: Superintendent, Government Press.

A Mirror of Hospital Practice

SPLENECTOMY FOR SPLENIC CYST

By F. C. FRASER

LIEUTENANT-COLONEL, I.M.S.

Distriet Medical Officer, Coimbatore

THE patient, a female aged 16 years, had noticed a swelling in the upper part of the abdomen for about two months; of late it had increased rather rapidly in size.

Examination revealed a large cystic swelling filling the left hypochondriac, epigastric, lumbar and umbilical regions. It was smooth and rounded in outline and did not cross the middle line; it was completely dull on percussion. Splenic tumour or pancreatic cyst was thought of, especially the latter as no notches could be felt on the border. Two weeks elapsed before an opportunity offered for operation and during this time the tumour grew rapidly, crossed the middle line and now filled the opposite (right) epigastric and umbilical regions. A skiagram after a bismuth meal taken at this time revealed the stomach lying in the right hypochondriac region, having been pushed across by the tumour.

The abdomen was opened through a paramedian incision in the left lateral line extending from the ribs to the umbilicus, and more room was obtained by a second incision running outwards in the transpyloric plane. An enormous cyst was found with a comparatively small spleen attached to its left border. Portions of the cyst were translucent and through one of these clear places, the cyst was tapped and about seven pints of clear fluid evacuated. As the cyst collapsed, the stomach came across to its correct position and it was then seen that the viscus was attached to the cyst by the gastro-splenic omentum, the included vessels being very short and plunging almost directly into the cyst. These vessels, the vasa brevia and the left gastro-epiploic, were ligatured with some difficulty owing to

the small space available, but a clamp put on to the adjacent collapsed cyst helped considerably. The cyst and spleen were then delivered from the abdomen and the splenic vessels secured and the lienorenal ligament divided—the latter being remarkably thickened and tough. Three small accessory spleens were left *in situ*, one was half an inch in diameter, the other two were only the size of peas. Doubtless they would grow in time and take on the function of the original organ.

The wound healed by first intention and the patient exhibited no signs of shock or any other untoward symptoms. She left the hospital two weeks later and is now, after a year, perfectly fit and healthy.

A CASE OF PURPURA RHEUMATICA (SCHONLEIN'S DISEASE)

By P. K. BANERJEE, M.B.

Ajmeer Road, Agra

THE patient was a Hindu female of the bania caste, and her general appearance was dull, pale and extremely emaciated. Her temperature was 99.8°F. , pulse—140, feeble and thready, and respiration—22 per minute.

Punctate petechial hæmorrhages, attended with slight temperature, appeared on the third day after the onset of menstruation; the hæmorrhagic spots were distributed all over her body and face, being more pronounced on the extremities, especially on the inner sides of the thighs. Next day bleeding from the mouth began, and she passed urine intimately mixed with blood. The rash was level with the skin, and when I saw her the colour had changed from pink to dark purple. The mouth was very sore and the gums were inflamed, hæmorrhagic patches being present on them. The tonsils were very slightly inflamed. The bleeding from the mouth was apparently from the inflamed gums. The throat was congested; lungs normal. The heart revealed a loud hæmic murmur in the pulmonary area, which may be attributed to the anæmia, the hæmoglobin value being 46 per cent. No gastro-intestinal symptoms were present. The bowels were constipated. The spleen was palpable and very tender on pressure. Vaginal examination revealed the cervix to be completely closed, so I concluded the bleeding was only from the urinary channels, either from the bladder or from the kidneys.

History of previous illness was negligible. There was no history of hæmophilia in the family.

The following treatment was adopted: Normal horse-serum, 10 cubic centimetres, was injected intramuscularly, followed by horse-serum tablets by mouth. The bladder was washed with hot boric lotion, followed by a hot lysol vaginal douche. Neotropin tablets were prescribed orally, *ter in die* and the mouth was swabbed with hexylresorcinol solution 1 in 1,000.

Next morning the general condition of the patient was better. Bleeding from the gums had completely stopped, but the urine was still mixed with blood, though it was less in amount. The temperature had gone up to 100.8°F. , and she started complaining of pains in the large joints. The same treatment was continued, except that the patient was put on salicylates 10 grains *ter in die*, as it was suspected that the purpura was of rheumatic origin. The salicylates had a dramatic effect and stopped the bleeding within the next 24 hours and the temperature touched normal, proving the case to be of rheumatic diathesis. The rash gradually disappeared within the next four days.

[Note.—The inflamed, sore gums which were the most prominent signs in the case suggest to us that scurvy was much more probably the condition present. There is also probably a connection between the injection of horse-serum and the onset of joint pains with a slight rise of temperature. We doubt the justification of basing a diagnosis of acute rheumatism on the effect produced by three 10-grain doses of sodium salicylate.

Also the claim that the salicylate stopped the hæmorrhage appears somewhat exaggerated in view of the fact that the horse-serum had already stopped the bleeding from the gums and had greatly reduced that from the bladder.—EDITOR, I. M. G.]

A VESICAL CALCULUS OF UNUSUAL SIZE

By B. N. KHANNA

House Surgeon, State Hospital, Junagad

A HINDU male, aged 43 years, was admitted into this hospital on 14th March, 1933, with symptoms of stone in the bladder. The bladder was sounded, and it was found that the stone was too big for litholapaxy. The alternative method of suprapubic lithotomy was suggested to the patient, but he refused operation and was discharged on the 20th March, 1933.

He was admitted again on the 11th May, 1933, and this time, was willing to have the suprapubic operation done. The patient was prepared in the usual way, and the operation was performed under chloroform anaesthesia by Captain P. T. Majumdar. An incision about three inches long was made from the top of symphysis pubis upwards in the middle line. The lower part of linea alba having been divided, the extraperitoneal tissues were separated. Two lateral sutures were passed through the bladder wall, and the already filled bladder was incised longitudinally. The gloved finger being put in, the enormous size of the stone was realized, and it was found to almost fill the bladder. In attempting to take it out, the thick crust of the stone was separated, and was removed piecemeal. The body of the stone was taken out later. The bladder wall and skin incision were closed and a *ter* inserted. The patient made an

The weight of the stone was 5 ounces 1 drachm.

A LARGE FIBRO-ADENOMA OF NECK

By BISHAMBAR NATH SIBAL, M.B., B.S.

In-Charge Civil Hospital, Mardan

A. S., a Pathan aged 60, presented himself at the out-patient department of the civil hospital,



Fig. 1.

Mardan, on 22nd February, 1933, having walked from Sakarga in Tribal Territory, a distance of

300 miles, to seek treatment for a large tumour growing from the right side of his neck.

The tumour, which by its weight and size was obviously causing distress, was supported by a cloth suspended from the patient's head. It was hard and nodular, freely movable over the subjacent tissues and had an ill-defined pedicle. It extended from the tragus of the right ear to within one inch of the symphysis menti (figure 1). Patient stated that he noticed a small lump in the skin over his lower jaw about the time his beard began to grow, over 40 years ago, and since then this lump had been gradually increasing in size. When asked why he had waited so long before seeking relief, he explained that he had no desire to risk his life by undergoing a surgical operation while in the flower of his youth, but that now being a grandsire and in the winter of his years he was prepared to take any risk to be rid of the discomfort of the tumour.

Patient was operated upon on 27th February, 1933. An elliptical incision was made round the base of the tumour which was easily removed *en masse*. The blood-vessels in the pedicle having been secured and ligatured, it was found necessary to remove some redundant skin, and the resulting scar was roughly Y shaped, the right arm and stem of the Y extending from the tragus of the ear to the symphysis menti below the mandible, in a natural crease of the neck. The left arm of the Y extended for about two inches transversely across the neck from the angle of the jaw. Recovery was uneventful. The wound healed rapidly leaving a healthy scar and patient was discharged on 22nd March, 1933, feeling very pleased with his improved appearance (figure 2).



Fig. 2.

The tumour weighed 4 pounds. A portion was sent to the Provincial Laboratory, Peshawar, for pathological examination, and was subsequently reported to be a fibro-adenoma.

I am indebted to Major D. V. O'Malley, O.B.E., I.M.S., Civil Surgeon, Mardan, who examined the patient and advised operation, and who gave me permission to publish the case.

A CASE WITH ABSENCE OF POLYMORPHONUCLEAR LEUCOCYTES

By S. P. GUPTA, B.Sc., M.B., B.S.

Demonstrator in Pathology, King George's Medical College, Lucknow

A. A., aged 26, Mahommedan male, was admitted to the King George's Hospital with the following complaints (1) pain in the abdomen, (2) masses in the abdomen and (3) occasional fever for four months. He gave a history of pain in the right testicle eleven years ago, and jaundice seven years ago. The first appearance of the abdominal tumour was preceded by severe pain in the left lumbar and hypochondriac regions. The patient felt the mass moving about in the abdomen and whenever it reached the hypogastric region he felt great discomfort and a sort of twisting pain. During attacks of fever of three or four days' duration the swelling of his abdomen used to enlarge.

The patient was anæmic but not emaciated. He had a coated tongue, clean teeth, and a thick and enlarged uvula. Definite, hard, lobulated, and movable masses were palpable in the right hypochondriac, umbilical and lumbar regions. Liver and spleen were not palpable. Inguinal, axillary, and cervical glands were not enlarged. Only a small gland was palpable in the left supra-clavicular region.

Though the possibility of Hodgkin's disease was never excluded the patient was kept on routine treatment for abdominal tuberculosis. He was afebrile for two weeks after admission, and his weight increased by one pound. In the first four days of the third week he had a temperature of about 101°F. and in the last three days it came down to normal. In the fourth week there was a similar rise of temperature. As the abdominal masses were enlarging, and becoming prominent, an exploratory laparotomy was suggested but it was not done on account of his low condition. In the fifth week the temperature again began to rise and reached 104°F. His pulse rose to 150 and respiration to 50 per minute. A blood count was done. Total leucocytes were 5,600 per c.mm., and a differential count showed lymphocytes 80 per cent, and large mononuclears 20 per cent. Polymorphonuclears were totally absent. Though the general outlook did not seem bad, the patient died the same day, and, unfortunately, no post-mortem could be held.

Comments.—Whatever the diagnosis may be, the point of greatest interest was the terminal blood picture. The absence of polymorphonuclear leucocytes has never before been noticed in this hospital. Such cases are rare in the literature too. Schultz first described this condition in 1922 under the term 'agranulocytosis'; and, as throat lesions were associated with it, Freidman suggested the title of 'agranulocytic angina', and as such cases without any throat lesions were described the term 'idiopathic neutropenia' was suggested. But, as some cases were definitely secondary, Schilling's 'malignant neutropenia' was considered to be the best name for this condition. For such a blood picture as was observed in our case 'absolute granulocytopenia' seems to be the most expressive. It is probably an end result of the action of some toxic agent, on the granulocytopoietic activity of the bone marrow.

As there were no throat lesions in the above case, it does not fall in the group of 'agranulocytic anginas'. His age, the chronic condition of the disease, and the absence of glands in the neck are against the diagnosis of glandular fever. Fever and matting of the abdominal tumours were certainly in favour of tuberculosis, but such large masses are rather rare in abdominal tuberculosis. On account of the chronic history and absence of myeloid changes in the blood picture, acute or chronic lymphadenitis or lymphatic leukaemia are excluded.

The most likely diagnosis is that of lymphadenoma, or as it has been lately called reticulo-endotheliosis. Jaffe has described a case.

of typical Hodgkin's disease with 800 white cells and 100 per cent lymphocytes. Our case is similar to that of Jaffe. The increase of monocytes to 20 per cent is more likely to be met with in cases of reticulo-endotheliosis than in tuberculosis. The absence of any myelocytes suggests that the absolute granulocytopenia was due to some toxic action and not due to a lymphadenomatous invasion and consequent metaplasia of bone marrow.

The other possibility is that of malignant endothelioma or Ewing's reticulum-cell sarcoma. But, as it has the histological characters of acute Hodgkin's disease this diagnosis is justifiable.

My thanks are due to Lieut.-Col. G. T. Burke, I.M.S., Physician to the King George's Hospital, for kindly allowing me to publish this case.

GONORRHOEA IN A BOY OF SEVEN

By A. R. MANSOOR, M.D., D.P.H.

University Hospital, Aligarh, United Provinces

THE occurrence of gonorrhoea in female children is fairly common, but the incidence of the disease in a boy is rare.

S. M., male, seven years old, was brought to me.

The history given was of burning during micturition, followed in a couple of days by the passage of a few drops of blood, and then a spurt of pus instead of the expected stream of urine.

On examination the meatus was found gummed up, and on separation a little thin purulent material was obtained on a platinum loop and a slide prepared.

The child's urine was clear and of a greenish tinge. I thought that probably he had infected himself with *B. pyocyaneus* by introducing something into the urethra.

However, on examining the slide pus cells and gonococci were seen in such abundance that there was no doubt of the diagnosis.

The method of infection was not ascertained but one of the male servants in the house was found suffering from acute gonorrhoea, so it is possible it was acquired accidentally from him.

[Note.—Abstracted by the Editor.]

A LEECH IN THE MALE URETHRA

By MON MOHAN GHOSH, L.B.Dr.

Medical Officer In-Charge, Kamalganj Dispensary, Sylhet

SOABULLA, aged 35 years, came to this dispensary on 10th November, 1932, and gave the following history:—

When washing jute in a pool of water he felt a pricking sensation in his penis. He came out of the water and was frightened to see that a big leech was entering his urinary canal. The leech entered the canal and disappeared as soon as he tried to pull it out. He came to the dispensary immediately and on palpation I felt a hard mass about one and a half inches in length in the urethra. The mass began to increase and the patient became very restless, he tried to urinate but could not pass any urine.

I first tried to pass a probe into the urethra but was unsuccessful. On the second attempt to seize the leech with a pair of sinus forceps I was successful and extracted it. Bleeding from the meatus continued for

some hours but by next morning it had entirely ceased and the patient had no further trouble.

I wish to thank Lieut.-Col. J. L. Sen, M.C., I.M.S., for his interest in the case.

ABILITY TO WALK A LONG DISTANCE AND GIVE DYING DECLARATION AFTER SEVERE HEAD INJURY*

By RUDR DUTT, L.M.S.

Assistant Surgeon, Dera Ghazi Khan

A HINDU adult male, after receiving severe head injuries, proceeded from one place to another in search of assistance, but failing to find any he finally went to the local police station and made a report as to how the injuries were received. The search entailed a walk of well over two miles.

The following injuries were found after death:—

On the right side of the head there was a large contusion covered with blood clot in the temporal region with a smaller one behind the ear. The right eye was displaced by a large orbital haematoma. He also had a contusion over the left parietal region.

There was a comminuted fracture of the right parietal bone, and a fracture of the base of the skull extending into the middle fossa, with rupture of the right middle meningeal artery and a large extra-dural blood clot. There was also a small contusion in the frontal area of the brain.

This case is reported on account of its importance from a medico-legal point of view.

PASSAGE OF A NEEDLE THROUGH THE ALIMENTARY CANAL

By V. KRISHNA MENON, L.M.P.

City Clinic, Chalapuram, Calicut

AT about six o'clock in the evening, 24th April, 1933, a girl, 12 years of age, was brought by her father, with a history of having accidentally swallowed an unthreaded sewing needle half an hour before. She had been made by her grandmother to swallow immediately a wad of cotton-wool.

After the throat was examined, she was made to swallow a piece of bread, which did not elicit any pain or irritation. Next she was given a full and heavy meal consisting of bread and plantains only, and kept under observation. Only solids were enjoined for the first twenty-four hours and a strict watch was kept on all motions passed thereafter.

From the 25th evening, she was allowed thick curds and on the following day a little milk also. One ounce of liquid paraffin was given in the forenoon of the 27th. Previously the girl had one motion on the night of the 24th, and three on each of the next two days. The second motion after the paraffin was washed through a sieve, and the needle was found blackened and with some encrustation—about seventy-two hours from the time of swallowing. It was an ordinary sewing needle about four centimetres in length.

Passage of a needle through the whole length of the alimentary canal must be a very rare occurrence hence this case has been reported.

* Rearranged by Editor.

Indian Medical Gazette

OCTOBER

THE PROBLEM OF LEPROSY

It is generally believed that leprosy is an infectious and contagious disease. This is of course the old traditional belief practically all over the world, and for many centuries there were in most countries laws and customs which aimed at preventing contact between healthy people and lepers. The medieval laws concerning lepers in Europe have often been quoted.

In the nineteenth century however the work of Danielsen and his followers challenged the belief in the infectiousness of leprosy and the result was a slackening of attempts at segregation of lepers in some countries. Towards the end of the nineteenth century when Hansen discovered the bacillus, the pendulum swung back again and while Jonathan Hutchinson's 'fish theory' caused a temporary diversion, the belief in the infectiousness of leprosy once more became general and there was a correspondingly increased effort to segregate lepers.

The country concerning which we have most accurate data is Norway, and the history of leprosy there may be summarized as follows:—

The disease was present in the middle ages; there was a leper hospital at Bergen in 1266, and others were established later elsewhere. By the end of the 16th century leprosy was reported as much diminished and most of the leper hospitals were closed; nevertheless the disease still exists. In 1839 there were 287 lepers in institutions and general interest in the reported increase of leprosy at that time brought about the appointment of a Royal Commission as the result of which more leper asylums were opened and 2,858 cases of leprosy were detected. In 1857 laws were passed to enforce segregation of cases in institutions or in the patients' homes. From that time there has been a steady decrease of leprosy in Norway, the official figures being in 1856 2,858, in 1875 1,752, in 1890 960, in 1900 577, in 1910 326, in 1920 160, and in 1930 69. Most of the cases now remaining are of very long standing and, during the five years 1926 to 1930, only three new cases were detected.

These facts appear to be conclusive proof of the efficacy of segregation, but there are two objections which may be made. The first is that this reduction is due very largely to improved social and hygienic conditions in Norway, and would probably have occurred without any segregation. The second is that, while such measures may be practicable in countries such as Norway with a comparatively small number

of lepers, with its considerable resources and with its educated population, they are impracticable in other countries where the number of lepers is much larger, the resources are less, and public opinion is uneducated. The first objection is difficult to refute and the second is undoubtedly true in some countries.

Nevertheless in some oriental countries, compulsory segregation has been tried, but the efficacy of the measure has not yet been conclusively demonstrated, and is still largely a matter of opinion. An interesting example is that of the Philippine Islands. In 1906 an island leper colony was founded and all detected lepers were induced, or if necessary compelled, to go there. This measure was hailed by some as being the death-knell of leprosy in the Philippines. The experiment has now been in progress for twenty-seven years and many practical difficulties have been encountered. There was much concealment of the disease, and this difficulty was possibly aggravated by harsh measures but, during recent years, a wiser handling of the patients has greatly helped in inducing them to undergo voluntary segregation. Also the institution of treatment, with the subsequent discharge of many patients on parole, has created a better feeling. Nevertheless it cannot yet be said that leprosy has been much reduced in the Philippines. What is lacking is the support of the segregation laws by enlightened public opinion. This is the great difficulty of all leprosy work in countries where education is comparatively undeveloped.

The problem of leprosy has been influenced by two developments which have taken place during the last few decades.

The first of these, the improvement in treatment, has attracted most attention. Treatment by injection of chaulmoogra and allied oils and their derivatives was started about 1890 and promising but not striking results were claimed by various workers; but later, technical improvements were made and from 1915 onwards far better results were claimed. Unfortunately, hopes too often were regarded as proved facts; improvement in the visible lesions was too often interpreted as indicating a cure. Stamping out leprosy by treatment soon came to be regarded by some as a possibility but there were many sceptics. Later, careful observers found that the results of treatment did not justify some of the claims that had been made. Others, failing to obtain striking results, went to the other extreme in their reaction against excessive optimism and stated that treatment was useless. This we consider to be a mistake. Treatment is far from being completely satisfactory, but under favourable circumstances in suitable cases it does produce improvement which is often permanent.

The other development, which has attracted less attention, but which may ultimately prove

to be more important than advances in treatment, has been in the greatly improved knowledge of the slighter forms of leprosy. In this development Indian workers can claim the greatest share. Many slight lesions in the skin, such as depigmented macules with slight anaesthesia, are now known to be due to leprosy although bacteriological examination is negative. We have found that this knowledge, which until recently was not common among medical men, was quite common among Indian villagers in some places. We have found that Indian villagers can sometimes diagnose leprosy at a stage when most doctors would fail to recognize it. Patients with one or a few such macules are very common in India and we know that many of these lesions undergo spontaneous arrest. Such cases are reported as being much less common in other countries. It is an open question whether this really is so, or whether they are present and are not being diagnosed. This certainly was formerly the case in India. It is now becoming generally recognized also that in endemic areas many people must become infected but never show any signs of the disease, and in fact those who develop the disease are probably only a fraction of the total number infected.

These two developments, the increase in our knowledge of the onset of leprosy, and the improvements in treatment, have markedly affected anti-leprosy work. The diagnosis of slight cases has led to a marked increase in the number of people reported as suffering from leprosy. The 1931 census reports an increase over the 1921 census of 44.2 per cent in the number of cases in India, and in some areas where leprosy propaganda work has been done the increase is over 100 per cent. These increases are probably more apparent than real, and are due to more accurate enumeration, although leprosy may be increasing in some areas, and it is probable that in India there are between one half and one million people showing definite signs of the disease.

Earlier diagnosis has also revealed the fact that only about one-third of the cases with definite signs of leprosy are discharging bacilli and are therefore considered infectious.

The development of treatment, although not doing all that was hoped and even claimed, has made a great difference to anti-leprosy work in India. The doctor and the health worker used to regard cases of leprosy as highly infectious and incurable, and hence the patient had no inducement to go to them for relief; but now we have treatment to offer, not a rapidly effective treatment it is true, but effective enough to bring patients in large numbers to doctors.

From the above outline it is obvious that the leprosy question has been in the melting-pot during the last decade. Various workers in many countries have expressed widely differing

views regarding the control of leprosy by segregation and by treatment. A leprosy commission of the Health Organization of the League of Nations was appointed to try to clear up some of the confusion. The first general session of the commission met in Bangkok in 1930 and was attended by authorities on anti-leprosy work from various countries. The report of this commission is a valuable document which discusses the principles of the prophylaxis of leprosy chiefly from an administrative standpoint. The Leonard Wood Memorial Conference on leprosy met shortly afterwards in Manila and the report of this deals with leprosy in its more technical aspects. This conference led to the formation of the International Leprosy Association and to the publication of the *International Journal of Leprosy*, the first number of which has recently reached us.

An attempt is now being made to apply in India the principles advocated by the Leprosy Commission of the League of Nations in their report, and, to consider this matter, a conference of leprosy workers from various parts of India was convened in Calcutta in March 1933, by the Chairman of the Indian Council of British Empire Leprosy Relief Association (Major-General Graham, O.B.E., C.I.E., I.M.S.). The resolutions and recommendations of this conference are published in this number of the *Gazette*.

There are two big organizations engaged in anti-leprosy work in India. The oldest is the Mission to Lepers which owns or aids no less than fifty-two leprosy institutions with accommodation for 8,400 patients. These institutions act as centres of segregation and treatment and to some of them are attached out-patient clinics which large numbers of patients attend; and some of them act as centres of training of doctors and others in anti-leprosy work.

The other organization is the Indian Council of the British Empire Leprosy Relief Association. This is a semi-official organization with branches in all the provinces. Its aims are to further research in leprosy, to survey the incidence of leprosy in India and to organize treatment and preventive work through out-patient centres.

There are in addition some institutions run by Provincial Governments, and work in out-patient centres organized by local authorities, by industrial concerns, and by private bodies. It is highly desirable that in India there should be a general policy of anti-leprosy work, in which all these various agencies may have their share. This policy the Calcutta conference has tried to formulate, not in great detail but in principle. The principles advocated by the conference should command general acceptance.

Anti-leprosy work should not be separated but should be an integral part of the general public health and medical work of the country. Leprosy cannot be controlled by treatment alone

nor by segregation alone, but a wise combination of these two measures may effect much more than either measure separately. Treatment brings the patients under observation, wins the confidence of the people and thus provides the opportunity for propaganda with a view to prevention. This propaganda helps to spread a knowledge of leprosy, which brings more patients for diagnosis and treatment. Leprosy clinics; in-patient institutions, leprosy hospitals and asylums all have their place, an important one in anti-leprosy work, but there is a need for co-operation and co-ordination of the work of different agencies. While many patients are not considered infectious and do not therefore need isolation, many are infectious, and the isolation of the latter is undoubtedly the most important step to be taken whereby to control leprosy. Isolation of all infectious persons in institutions is impossible but accommodation should be available for all those willing to undergo voluntary isolation. The institutions of the Mission to Lepers perform an important service in providing such accommodation but it is not nearly adequate to meet the needs, and more such institutions are undoubtedly needed. Many patients are not willing to submit to voluntary isolation and the only available method of procuring their segregation is, by teaching, so to educate public opinion that isolation in their homes and villages is insisted upon by the villagers themselves.

The resolutions of the Calcutta conference advocate the setting up of non-official leprosy boards in endemic areas, in order to arrange

for co-operation between the different bodies engaged in anti-leprosy work. They advocate the more thorough organization of training of doctors and health workers, and the establishment in endemic areas of special leprosy clinics to act as centres of treatment, of preventive work and of training for medical men. In addition leprosy clinics in general hospitals should be encouraged.

The need of increased accommodation in in-patient institutions for infectious cases of leprosy is emphasized. The need of further research is recognized, and the organization of epidemiological research in a rural centre is advocated. The importance of examination of school children and labourers in industry for signs of leprosy is stressed. The recommendations of the conference also cover such subjects as the importance of general treatment, the most effective forms of special treatment, the need for observation and after-care of quiescent and arrested cases, the employment of non-infectious patients, and the question of non-infectious cases in school children.

The conference has already borne fruit in that the Surgeon-General of the Madras Presidency has called together a leprosy conference of medical and social workers at which the findings of the Calcutta conference were considered and arrangements were made for putting many of its resolutions into effect.

This Calcutta conference should be a landmark in the history of leprosy in India and will we hope help greatly in the development of anti-leprosy work along sound lines.

Special Article

THE EARLY SIGNS OF MENTAL DISORDERS

By OWEN BERKELEY-HILL

LIEUTENANT-COLONEL, I.M.S.

Medical Superintendent, Ranchi European Mental Hospital

INSTRUCTION in the early signs of mental disorder does not receive anything like the attention it deserves in medical schools and colleges in this country. Teachers of psychiatry still devote far too much time to expositions of full-blown psychoses. A glance at the majority of the syllabuses on psychological medicine or at the type of questions set in examination papers will corroborate this statement. No doubt instruction in the psychoses is not wholly without interest but for the majority of medical students the interest is more theoretical than practical because only a small percentage of medical students has any intention of becoming alienists. What the general practitioner, not

to mention the specialist in medicine, surgery and gynaecology, wants or should want to know, is the early signs of mental disorder in their own patients. Frequently practitioners of medicine, surgery, gynaecology and so forth are so ignorant of what constitutes mental disorder that they fail to recognize it when it is staring them in the face.

Before we proceed to consider the early signs of mental disease, it will be not without advantage to pause for an instant to try and formulate some idea as to what constitutes mental disorder of any kind whatsoever. The world is becoming daily fuller and fuller of books dealing with mental phenomena of every conceivable variety but how few appear to take into consideration the enormous complexity of the problems with which they deal, but carry on in such a light-hearted fashion that even the least sceptically-minded of us may well wonder what on earth it is all about. To give a satisfactory definition of any disease is no easy

matter. Indeed, a definition of what constitutes 'disease' is generally omitted in textbooks of medicine and surgery. The omission is ominous. The same observation holds good for textbooks on mental disease but here there is some excuse for the omission because to establish the existence of mental disease we have no other standard to go upon than social convenience. This is highly arbitrary, hardly less so than our judicial code. People consult mental specialists when they are either intolerable to themselves or to other people. In the latter case some form of coercion is generally necessary to bring the consultation about.

Let us suppose that a change takes place in our social conditions, whereby a type of mental disorder which is now regarded as intolerable becomes innocuous or even advantageous. What will happen then? It is one thing to say that we will get rid of one kind of mentality because, under existing conditions, it is unendurably tiresome, and quite another to say that this or that type of mind is in itself wholesome or unwholesome. Primitive types of mind are regarded as insane whenever they appear in a so-called civilized society. On the other hand, it seems quite likely that the average citizen of London to-day would have been counted at least mentally defective had he appeared in ancient Athens. In the same way, if a man of the future has ever been born into this twentieth century of ours, he may very well be in an asylum or a jail now.

One of our main difficulties is that we only know very roughly and uncertainly what we do not want of the human mind. As to what we ought to want—will such knowledge ever be possible? Would it, we may ask, have been safe to have allowed a mental specialist to pass an opinion on the mental condition of many great men of the past—John Bunyan, Jonathan Swift, William Blake, Thomas De Quincey, Samuel Coleridge, Percy Bysshe Shelley and Edward Thomas, to take a few examples from eminent men of letters? Our modern psychotherapists might very well have cured Bunyan of his terrible anxiety states about religion, and Shelley of his atheism. The fierce bitterness of Swift might to-day be analysed away and 'treatment' of various sorts might have made it unnecessary for De Quincey and Coleridge to remain morphia addicts and Thomas to renounce alcohol. A course of occupational therapy might have stopped for good those wonderful visions of Blake. But had these 'treatments' been carried out with what psychotherapists nowadays would deem success, what would have been the effect on English literature? Would it have been deprived of 'Pilgrim's Progress', the 'Tale of a Tub', 'Songs of Innocence', the 'Confessions of an Opium Eater', the 'Ancient Mariner', 'Adonais' and 'Like the Touch of Rain'? It seems not improbable. As the author of 'Sisyphus', that amusing

satire on psychology and its exponents, observes: 'It is chastening to reflect that the persons we most admire in past ages were often those who were, in their own day, the least at home in the world'.

The founder of Christianity was so little adapted to the age in which he lived, that he got himself executed as a common criminal. Yet Christianity could never have existed had he not been executed. On the other hand, as Jung has pointed out, an individual well adjusted to a mistaken society may perish with it. If it were adaptability rather than adaptedness that were in question, the ideal would be more understandable. But when all has been said on this point it is in a limited sense to every one's interest that they should be as well adapted as possible to their particular position in life.

On this assumption we may now pass on to consider the theme with which this paper is primarily concerned, namely, the early signs of mental disorder. First, and by far the most important as a sign of mental disorder, is a permanent change in the behaviour, because a change in behaviour means a change in temperament and character. But not all permanent changes in behaviour connote insanity. A Christian who becomes a Mahomedan, or a Mahomedan who turns Christian is not necessarily exhibiting signs of a disordered mind by so doing. St. Augustine, the greatest of the Latin Fathers of the Church and one of the foremost scholars of his age, could hardly be held to have been mentally disordered when he embraced Christianity and was baptized at the age of 33, when up to then he had led what is commonly termed an immoral life and had been a prominent member of the sect of Manichæans who worshipped the devil. No, the change in behaviour which generally connotes some mental disorder is generally a change for the worse, not for the better. A quiet, placid, kindly nature becomes, with the onset of insanity, moody, taciturn, sullen, quarrelsome or even cruel. A truthful individual whose mind is diseased may take to lying and a modest person may turn into a boaster and braggart. A clean, tidy, well-groomed man may become dirty, with the onset of insanity. He ceases to pare his nails or to have his hair cut as heretofore. He omits to shave or bathe himself properly. He may neglect his family as well as himself. Sooner or later he neglects his business. He may take to alcohol or drugs of some sort. A sociable man may suddenly become shy to the extent of avoiding the company of others and keeping as much as possible to himself. Mental disorder may be ushered in by loss of sleep or loss of appetite, or both. A thrifty man may suddenly become extravagant. While hitherto accustomed to order a single suit of clothes at a time, he now places an order for a dozen suits.

Hitherto accustomed to go to his office on a bicycle or in a public conveyance, he takes suddenly to taxis or even buys a car of his own. A devout man, hitherto regular in the practice of his religion, suddenly ceases to pray or read the Scriptures. He may go so far as to brag openly that he believes in nothing, that all religion is nonsense and that what the world wants most is colleges for the instruction of young men and women in atheism. A devoted husband may desert his wife or introduce a strange woman into his house as his mistress. A kind and loving father takes to ill-treating his children, calling them brats and turning them into the street. Last of all, the mental disorder may lead to the commission of a crime of some sort, and that generally one of violence.

Most doctors are aware nowadays of the marked deterioration, frequently of very sudden onset, that occurs in children who have suffered from encephalitis lethargica (sleepy sickness). Well-behaved, truthful and industrious children become troublesome, lazy and boisterous and frequently take to lying. Such children very often come into collision with the law as they often commit offences, particularly that of stealing. In short, a doctor, who sees a man or a woman or a child, with whose temperament he is well acquainted, beginning to exhibit traits of character other than those he has observed hitherto, should suspect the presence of some form or other of mental disorder. In the case of a child, a doctor would only be doing his duty in bringing the matter to the notice of the child's parents. In the case of an adult the matter is more delicate, because the great majority of people still regard mental disorder

in the same light as cancer and venereal disease were regarded fifty years ago, that is, as something too dreadful to talk about. Hence it is sometimes by no means easy to tell a man or woman that he or she is showing symptoms of insanity. Good intentions of this description often meet with violent opposition. However, where there is a will there is often a way, so that a doctor, who appreciates fully the importance of early treatment in mental disorder, should be able, somehow or other, to persuade the afflicted person to consult a specialist. If this is in no way possible, it is the doctor's duty to bring the state of affairs to the notice of some near relative and recommend that appropriate measures be taken without delay.

In matters of this sort it is evident that a doctor, who is not a trained mental specialist, must depend more on intuition than on knowledge. Indeed, in almost any branch of medicine the most successful practitioners seem to be those who realize that to understand human nature it is not enough to study what scientists can tell us. 'The possible twists in the maze of consciousness', says the author of 'Sisyphus', 'are endless and no psychologist is ever likely to find his way through them, however many trials and errors he may make'. A psychologist may try to escape consciousness, as does the founder of the Behaviourist school of psychology, by denying its existence, but few have the courage or the blindness for that counsel of despair. As the author of 'Sisyphus' says, 'it is only the artist, edging towards the mystery, darting from tree to tree, catching glimpses instantly lost again, who can begin to show us something of our own uniqueness'.

Medical News

WORKMEN'S COMPENSATION IN INDIA NEW PROVISIONS

WE have received from the Calcutta Claims Bureau a copy of a pamphlet, recently issued, containing a summary of the important proposed amendments to the act contained in the new Workmen's Compensation Amendment Bill, as finally amended and approved of by the select committee of the Legislative Assembly. Alongside each proposed amendment is shown the existing provision, if any, under the act so that employers of labour and other persons interested in workmen's compensation matters may see at a glance the changes likely to be made as compared with the existing legislation, when the new bill is finally passed into law.

The pamphlet explains the many radical changes which are foreshadowed in this important piece of legislation and it also contains two comparative tables showing the benefits under the existing act and the benefits now proposed under the bill for each of the wages classes. A comprehensive list of persons who will be deemed to be 'workmen' under the new legislation has been included.

Workmen's compensation is a subject which concerns practically every large employer of labour and many new classes of employees, to whom the act has not

hitherto been applied, will now shortly be brought within the scope of the legislation.

We recommend that every employer should acquaint himself with these provisions by obtaining a copy of this pamphlet either direct from the Calcutta Claims Bureau, 26, Dalhousie Square, Calcutta, at a cost of annas eight per copy, or from any of the leading insurance companies.

THE CEYLON SANITARY INSPECTOR

WE have received a copy of the first issue of a new journal *The Ceylon Sanitary Inspector*. This number is really a report of the proceedings of the first conference of District Sanitary Inspectors, which includes several papers on matters of interest. No doubt this journal will be of use to the sanitary inspectors of Ceylon as it will provide a medium whereby they may discuss their problems. There is no mention of how often it is proposed to publish this paper, what is its price, where it may be obtained nor who publishes it. If it is hoped to obtain a circulation outside the circle of the Ceylon sanitary inspectors themselves we would suggest supplying the above information on the cover of the next issue.

FIFTY YEARS AGO

(From the *Indian Medical Gazette* of October, 1883, Vol. XVIII, pp. 265, 271, 272 and 283)

CAN CHOLERA BE GENERATED *DE NOVO*?

By SURGEON-GENERAL S. C. TOWNSEND, C.B.

In my paper on the 'Variations in the incidence of cholera', which you were good enough to publish in the numbers for March and April, after adducing evidence that the degree of incidence on a unit of population was determined by the condition of its water-supply, I pointed out that even if this were conceded there would still remain, for further enquiry, the nature of the relation between impure water and the primary or essential cause of cholera, and that one of the questions to be decided was whether cholera could be generated in water *de novo*. I have always held it possible that cholera might be so generated under favourable atmospheric conditions, but in the very large number of outbreaks which I have investigated in the course of the last ten or fifteen years, the instances in which importation of infective material by human intercourse was not a more probable immediate cause of the outbreak have been very rare. An outbreak, however, of a disease which at all events closely resembled cholera recently occurred in the Lahore district, under circumstances which afford no ground for suspecting importation, and as it has on this account an important bearing on the above question, I trust you will favour me by giving a place in the *Gazette* to the following report, and also to the descriptions of two outbreaks which were severally the first appearances in wide tracts of country of the great epidemics of 1868-1869 and of 1875-1876 in Central and Western India.

The history of these three outbreaks illustrates the difficulty of solving the question whether cholera is ever generated *de novo*. In the first instance there was no ground for suspecting importation, but there is want of certainty that the disease was true cholera. In the other two instances probability of importation, though slight, cannot be altogether excluded, but inasmuch as they were isolated outbreaks, or first outbreaks after long intervals of freedom from epidemic prevalence, the probability is great that the conditions under which they occurred are those under which cholera is generated if it ever is generated *de novo*. The conditions present in all the three outbreaks above described were intense heat and great dryness of atmosphere, and water used

for drinking in which organic impurities were highly concentrated; in the two outbreaks last cited, the death of the fish and their subsequent putrefaction probably gave greater intensity to the views.

August, 1883.

ON ENTERIC FEVER

By SURGEON W. E. SAUNDERS, A.M.D.

MUCH enteric fever is classed under that great cloak for our ignorance, the term simple continued fever; but it would be far better if we had the courage of our opinions and called all suspicious cases of fever, lasting over two days, by their correct name; lest, by neglecting to do so, we tempt the attendants to be careless as to the disposal and disinfection of the stools, and so give rise perhaps to fresh cases and a spread of the disease. We must act on our own experience, or we may be led astray; for instance the majority of our leading physicians consider milk the best diet in fevers, especially if the bowels are affected, but Hippocrates did not allow milk to be used particularly in the latter cases. We must be careful, therefore, to place no blind adherence to the old masters or fathers of medicine, but act as our own experience leads us to consider best.

To a great extent successful physicians hold a despotic sway over their professional brethren, and a doctrine introduced by an outsider as it were in the investigation of a disease, one phase of which only is common in England, finds that, after years of research, the doctrine evolved obtains little hearing, and the truth in fact runs the risk of being almost crushed by the authority of a few great names, as happened with the ipecacuan treatment of tropical dysentery.

If all Army Medical Officers were to record their experience in enteric fever (for, being extended as it is to all parts of the world, it must be unequalled) they could add much to the knowledge of this disease. Difficult as it is, owing to frequent moves, to give our experiences to the professional world in anything approaching a complete form, still we might all of us by recording facts, and not merely our deductions and impressions, convince our professional brethren, who are not so fortunate as to have seen this disease in all parts of the globe, that there is yet much to be learnt regarding the ætiology at least of enteric fever.

We estimate our knowledge of disease too highly, and though few are willing to own it, medical science is really still in its infancy.

Current Topics

Treatment of Menstrual Irregularities

By WILFRED SHAW, M.D., F.R.C.S., F.C.O.G.

(Abstracted from the *British Medical Journal*, 27th May, 1933, p. 907)

THE type of patient now under consideration is the woman who has some form of menstrual irregularity independent of the presence of either tumour or inflammation of the pelvic organs.

EPIMENORRHOEA

In this form of menstrual irregularity the patients menstruate with a cycle less than the normal twenty-eight days—usually with one of twenty-one days or with one of fourteen. Typically the menstrual cycle is constant, and is not irregular. In some cases, in addition to a reduction in the menstrual cycle, the duration of the hæmorrhage is prolonged and the amount lost on each day is increased. This clinical form of menstrual irregularity is very common, but it must be emphasized that epimenorrhœa in itself is not a disease but merely

a symptom. Cases of epimenorrhœa can be classified into fairly well-defined groups. The post-partum type is seen very often indeed, and when such patients start menstruating after parturition the cycle is reduced from one of twenty-eight days to one of twenty-one or fourteen. Post-partum epimenorrhœa may, of course, complicate inflammation of the Fallopian tubes and ovaries, but such cases are relatively few, and in the common form no lesion can be detected in the pelvis. As I have already stated, these cases are probably related to a disturbance of the endocrine balance, and are perhaps due to over-activity of the anterior lobe of the pituitary.

Epimenorrhœa occurs most frequently, however, in patients about the age of 45, when they are approaching the menopause. It is almost invariable that the amount of blood lost at each period is excessive, and quite often leads to a severe degree of anæmia. Not seldom the uterus is found to be enlarged, and is harder than normal. Until recently such cases were grouped under the term 'chronic metritis', but since the advance in

our knowledge in the physiology of menstruation it has become generally recognized that both the epimenorrhœa and the uterine hypertrophy are due to over-activity of the ovaries. Epimenorrhœa is also common in cases of fibroids, particularly in patients over the age of 40. In another group it develops in patients about the age of 35, most of whom are single. Sometimes it is associated with salpingo-oöphoritis, and sometimes with chocolate cysts of the ovary. The ætiology of these cases of epimenorrhœa is not known with certainty. At the present day it is generally accepted that it is not related either to an inflammation of the appendages or to any local lesion in the uterus itself. Almost certainly the condition is due to an abnormality of ovarian function, although there is no proof that the primary fault lies in the ovary; it may very well be that the pituitary is primarily responsible.

Treatment

The treatment of epimenorrhœa is one of the most difficult problems in gynecology. One has to deal, not with a diminution of activity for which an appropriate hormone might reasonably be administered, but with over-activity, and the question is essentially one of inhibition of ovarian activity. Now, it is quite clear that whatever pharmacological properties may be claimed for the various ovarian and pituitary hormones, no one has at any time suggested that any one of these has an inhibitory effect on the ovary. For these reasons one is very sceptical as to whether the administration of any ductless gland preparation is likely to be of benefit in a case of epimenorrhœa. These theoretical considerations are borne out by my own experience, and I have personally given both œstrin and the anterior pituitary hormones to cases of this kind without result. When we turn to the prescription of drugs in the treatment of epimenorrhœa it is clear at the outset that there can be small hope of success. The only way in which such drugs could act is by inhibiting ovarian activity. It is true that the amount of blood lost during each period can be controlled by drugs such as ergot and by proprietary preparations such as femergin, but it is difficult to conceive that there is any drug on the market which possesses the remarkable property of inducing a specific inhibitory effect on the ovary. Again these theoretical considerations are borne out by clinical experience. The question now arises as to what can be done for these cases. In patients of 45 or over treatment as a general rule resolves itself into the creation of an artificial menopause. The patient is anesthetized, the uterus is curetted, and then a tube containing 50 mg. of radium is inserted into the uterus and kept there for forty-eight hours. This is an excellent remedy so far as the uterine bleeding is concerned. It is true that the results are often not immediate, and patients occasionally have one or two periods after the application of radium; but it is very exceptional for further bleeding to take place. Sometimes the first hæmorrhage after radium is copious, because the radium itself produces a local inflammation in the endometrium, and this hyperæmic area bleeds excessively during the menstrual period. There are two other objections to radium treatment: one is that almost invariably there is a persistent vaginal discharge due to the local inflammation of the endometrium, and the second is the onset of menopausal symptoms. After the age of 45 severe menopausal symptoms as the result of the creation of an artificial menopause by radiological means are not usual, although they are extremely common under the age of 40 and fairly common between the ages of 40 and 45. It is difficult to give an opinion as to whether the patient is likely to develop these menopausal symptoms if an artificial menopause is brought about; and if the patient is a good subject for an operation, with a thin abdominal wall, I often prefer hysterectomy with conservation of the ovaries to radiological treatment. It should be emphasized that with modern technique hysterectomy has a very low mortality, and if a patient survives the operation and has her ovaries retained she

is much more likely to be free of symptoms than if an artificial menopause is induced radiologically. So far as x-ray treatment is concerned, the end-results are similar to those obtained after the application of radium. The great drawback to x-rays, however, is that for sound therapy the uterus should be curetted prior to treatment, so that carcinoma of the body of the uterus or of the isthmus can be excluded.

Whereas the treatment of epimenorrhœa in patients approximating to menopausal age is fairly successful, that in younger patients is extremely difficult. Both x-rays and radium are, in my view, contraindicated as a means of producing a permanent artificial menopause, which in patients younger than 40 almost invariably leads to appallingly severe menopausal symptoms; and one of the worst sequels is the development of kraurosis vulvæ, with its attendant symptoms of pain and dyspareunia. Cases of this sort are sometimes encountered, and it is not an exaggeration to say that the resultant symptoms often produce more distress than the original epimenorrhœa. Theoretically the induction of a temporary artificial menopause with either x-rays or radium would seem a satisfactory procedure, but in practice this is not so. The essential difficulty is to obtain the correct dosage, for if a small dose is given no effect is obtained, while if it is too large the result is a permanent artificial menopause. The margin is small, and experience at St. Bartholomew's Hospital has shown that it is extremely difficult to gauge with any accuracy the correct dosage for a temporary artificial menopause. My own view is that with x-rays so many factors—such as the location of the ovaries and the thickness of the abdominal wall—have to be considered that this form of treatment is unlikely ever to be used extensively: similarly with radium. I believe that the effect of radium is upon the ovary and not upon the uterus; and, again, it is difficult to gauge the exact distance of the ovaries from the radium placed within the cavity of the uterus.

The treatment of epimenorrhœa in patients prior to the age of 40 resolves itself into either expectant treatment or operation. In cases of post-partum epimenorrhœa experience shows that almost invariably the menstrual functions right themselves spontaneously in due course. Indeed, it is very rare to see patients who give a history of epimenorrhœa which has persisted for more than three years following childbirth. In these cases, provided the patient does not acquire a severe degree of anemia, the administration of such drugs as ergot during the menstrual period, combined with rest, is the wisest course to follow, and the return of the normal menstrual cycle should be awaited. In the other cases of epimenorrhœa the position is difficult. In those in which it arises without obvious cause in single women of the age of 35, clinical experience shows that it is exceptional for them to return to the old cycle of twenty-eight days. Whether operation is performed depends solely on the degree of anemia. If operation is decided upon the correct procedure is to perform subtotal hysterectomy and to leave the ovaries behind. It is quite clear that this method is drastic, and it is warranted only if the patients suffer from a high degree of anemia. The results of hysterectomy are extremely good: the primary mortality is low and the end-results are eminently satisfactory.

METROPATHIA HÆMORRHAGICA

The recognition of this disease is the outcome of researches on the menstrual cycle. The full description of the pathological conditions is due to Schroeder as a result of his investigations carried out at Rostock during the war. The disease is characterized by a complete upset of the menstrual functions, so that ovulation is inhibited and corpora lutea are not produced in the ovaries. Always a cyst is found in the ovaries, and has the structure of a cystic ripening follicle. The condition of the endometrium is that of a diffuse polypoidal hyperplasia, and large plum-coloured polypi project from the endometrium downwards towards the cervical

canal. The endometrium shows the changes of a true hyperplasia combined with cystic dilatation of the glands, and in the superficial layer large areas of necrosis can be observed. Premenstrual hypertrophy never develops in the endometrium because a corpus luteum is not found in the ovaries. Metropathia hæmorrhagica is not uncommon, and can be diagnosed with a fair degree of precision if due care is taken. It occurs most frequently about the age of the menopause, but it is also seen in young girls before the age of 20, and it is not unusual before the age of 30. The symptoms are fairly characteristic. Usually the patients give a history of a short period of amenorrhœa; this lasts for about six to ten weeks and is followed by continuous bleeding, which may persist for many months. (I have seen cases in young girls in which it has gone on for years.) The amount of blood lost on each day is not excessive, and it is rare for large clots or severe bleeding to be seen at any stage of the disease. The characteristic symptom is continuous bleeding, similar to the hæmorrhage of a normal menstrual period.

The treatment of metropathia hæmorrhagica corresponds almost exactly with that of cases of epimenorrhœa, with the exception that in the former we have to deal sometimes with young patients—patients below the age of 25. In these cases the first procedure to be employed is curetting. The whole of the endometrium should be carefully scraped away and the material removed examined microscopically so that the diagnosis can be confirmed. The results of curetting are not very satisfactory, and in most cases the continuous bleeding recurs within a few months; nevertheless, it is sometimes stopped and the normal menstrual cycle returns. There is, however, a tendency, even in these cases, for the disease to recur, and it is very interesting to notice that a cyst may form in the opposite ovary. In young patients with metropathia hæmorrhagica, if curetting fails the next line of treatment is to give anterior pituitary hormone either in the form of the prolan preparations or of Parke Davis's 'antuitrin S'. This method has been employed extensively in America and in Canada, and encouraging results have been reported; in my hands, however, they have not been good. Theoretically, this therapy follows the correct line, for the object of the administration of the anterior pituitary hormone is to stimulate the ovaries to produce corpora lutea. It may be that when more potent preparations are available this form of treatment will be generally adopted. In a few cases I have tried the application of small doses of radium of the order of 40 or 50 mg. for periods varying from twelve to twenty-four hours, but again I have not had any satisfactory results. This, again, is theoretically sound, for it aims at creating a temporary artificial menopause, but, as in all such cases, the essential difficulty is to give the correct dosage.

It might be thought that removal of the ovary which contains the cyst would lead to cessation of the symptoms. A fair amount of evidence has accumulated to show that the opposite ovary invariably becomes cystic within a short space of time, and the continuous bleeding recurs. Unfortunately, in young patients, if there is no response to the various treatments I have indicated, one is sometimes forced to perform hysterectomy and to leave the ovaries behind. It is obvious that such a procedure is very drastic and not to be lightly undertaken. In my experience the patient and her relations eventually insist upon the removal of the uterus, for it is not uncommon for a severe degree of anæmia to be produced by the continuous bleeding; the patient and her friends become tired of the unsatisfactory results of the methods employed, and she becomes insistent upon having the uterus removed.

HYPOMENORRHEA

In this type of menstrual irregularity the menstrual cycle is prolonged. The usual history given is that the patient menstruates every six weeks, and then perhaps every three months; she may then have a period of

amenorrhœa lasting for six months or even longer. Irregularity of the cycle, in which there is a wide interval between the menstrual periods, is a characteristic of hypomenorrhœa. It is seen most commonly in patients about the age of 30. So far as the menstrual functions are concerned, the cause of hypomenorrhœa is an irregularity of ovarian function, and histological investigations prove that ovulation and corpus luteum formation occur spasmodically. Two types can be distinguished: one in which the fault is primarily ovarian, and the other in which the fault lies in one of the other ductless glands, usually the pituitary; the ovaries are deficient secondarily. Patients with primary ovarian deficiency give a history of a late onset of puberty and irregular menstruation from the beginning; such patients frequently have spasmodic dysmenorrhœa, and not seldom are sterile. In addition, there are certain physical signs of primary ovarian deficiency, such as an ill-developed uterus, small vagina, and scaphoid perineum. On the other hand, cases of secondary involvement of the ovaries usually give a history of normal onset of puberty without severe spasmodic dysmenorrhœa, and quite commonly the patients have borne children prior to the onset of the menstrual irregularity. There are all varieties of endocrine disturbances leading to hypomenorrhœa, and I do not propose to go into them in any great detail. A common type is that in which the patient about the age of 30 develops adiposity, headaches, and irregular and scanty menstruation.

In all cases of primary ovarian deficiency, treatment should be directed along the lines of organotherapy. The results obtained are far from being satisfactory, but occasionally dramatic improvement has been reported. Of the ovarian hormones, œstrin is marketed in the forms of theelin, progynon, menformon, and sistomensin, and recently the British Drug Houses has put a more potent preparation on the market, 'œstroform'. Œstrin should always be given subcutaneously, for it has been calculated that subcutaneous injections are eight times more powerful than the same dose given orally. This leads to the inconvenience of a hypodermic injection. Another disadvantage is that only small doses are put up by the manufacturing chemists, and it is difficult to believe that any dose of the order of a hundred rat units is likely to have any lasting effect on an adult woman. If such doses are given they must be administered frequently, probably at least three times every week. The corpus luteum hormone, progesterin, is not marketed at present, so that so far as ovarian therapy is concerned only œstrin is available. On theoretical grounds the anterior pituitary hormone, by stimulating the ovaries to produce ripening follicles and corpora lutea, is to be preferred to the ovarian hormones themselves. The pituitary preparations that are available are the prolan preparations and antuitrin S. It should be remembered that here again the hormone must be given by injection, and it is essential that the substances should be freshly prepared. With the anterior pituitary hormone there is the same difficulty about dosage. Probably the ampoules that are put up by the manufacturing firms do not contain sufficient of the active principle to have any lasting therapeutic effect. In any case, if the injections are to be given they must be given frequently—at least three times every week. I carried out some clinical trials with œstrin some years ago and found that in cases of primary ovarian deficiency a good effect was obtained only in those of mild degree. There was little evidence that it had any good effect in severe cases, and I believe that this view is generally held at the present time. With the anterior pituitary hormone the results are not perfectly satisfactory, and it is wrong to suppose that the hormone has a specific effect in reducing the irregular cycle of cases of hypomenorrhœa to the normal cycle of twenty-eight days. In some instances of hypomenorrhœa, in which the patients also complain of sterility, dilatation of the cervix may be beneficial. For some reason or other dilatation of the cervix stimulates the generative organs and, as is well known, conception

frequently follows this procedure. Similarly, in cases of hypomenorrhea the menstrual cycle may revert back to its regular rhythm. This treatment is frankly empirical, and is based on clinical experience. Nevertheless, it is a valuable therapeutic measure in cases of hypomenorrhea, particularly if sterility is an attendant symptom.

Air Traffic in Relation to Public Health

By T. H. D. GRIFFITS

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XIII, No. 3, May, 1933, p. 283)

At repeated sessions of the Permanent Committee of the International Office of Public Hygiene problems of the sanitary control of air navigation have received consideration, and it has increasingly become apparent that any set of just and reasonable regulations must be predicated upon facts established through researches and studies of factors relating to air traffic.

Realizing the necessity for investigations on the subject, the United States Public Health Service began on 23rd July, 1931, the inspection, for the presence of mosquitoes aboard, of all aircraft arriving at Miami, Florida, from foreign and insular ports. Strangely enough, the first mosquito caught was an *Aedes aegypti* (male) on 28th July, on the ship coming from San Salvador. From 23rd July to 12th September, 1931, there were 102 inspections of airplanes just arrived at Miami from points in Panama, Central and South America, the West Indies, Cuba and Mexico. On these planes a total of 29 mosquitoes was captured: one *Aedes aegypti* and twenty-eight *Culex quinquefasciatus*. Later inspections during the seasons of 1931 and 1932 have added to this list specimens of six other species.

This preliminary work in itself was sufficient only to determine the fact that mosquitoes were carried for some distance in aircraft of three different types—Trimotor Fokkers, Commodores and Sikorsky Amphibians. There was not established, however, anything definite as to how far these mosquitoes had travelled by airplane or how long they had remained aboard. In order to secure more definite information on these points, the United States Public Health Service carried out an experiment by staining and liberating *Aedes aegypti* on passenger planes of the Pan American Airways System at San Juan, P. R. Briefly the experiment and results were as follows: Several hundred *Aedes aegypti* were developed from larvae collected in San Juan and after feeding those that would take blood from the arm, batches of the adults (male and female) were stained with a 2 per cent solution of eosin in water, using a small atomizer to apply the stain through a gauze-covered cage. These specimens were liberated from the cage in all compartments of the 10 passenger Trimotor Fokker planes immediately before leaving for Miami, Florida, on 13th, 16th and 18th September. The time of leaving San Juan on each of these days was about 5-30 in the morning and arrival at Miami was approximately 4 o'clock in the afternoon, with an aggregate of about one and a half hours for stops at Santo Domingo, Port au Prince and Camaguey. The speed was approximately 125 miles per hour, and the maximum altitude reached on the flight about 5,000 feet. Each of these airplanes carried into Miami stained specimens put aboard at San Juan on the morning of the day of arrival in Miami. In the three experiments 100 mosquitoes were liberated on the planes at San Juan and 22 were captured after landing and unloading passengers, mail and baggage at Miami. It is, of course, possible, or even probable, that even a larger percentage of the mosquitoes put aboard came through, for one is not sure of having seen all mosquitoes and it is not always easy to catch all specimens seen. By these exact experiments, the first of record anywhere in the world, it was demonstrated that cabin planes carried mosquitoes for ten hours or more and for a distance of 1,250 miles.

Renewing the studies of last season, and adding more rigid tests of the capacity of *Aedes aegypti* to travel by airplanes, the United States Public Health Service, while continuing the routine inspection of planes for mosquitoes at Miami and inaugurating similar inspection service at Brownsville, Texas, undertook another series of staining experiments which was carried on, first from San Salvador, Central America and, later, from Cristobal, C. Z. The latter studies are still in progress.

Through hearty co-operation of the Pan American Airways System experiments on stained mosquitoes liberated on airplanes at San Salvador and destined for Brownsville, Texas, were begun by the writer at San Salvador in the latter part of April 1932. Reports are complete on the loading of 12 airplanes at San Salvador and the inspection of these planes at Brownsville. In the twelve batches of mosquitoes, total number of insects 840, liberated in all compartments of the planes, 69 specimens were captured on the planes at Brownsville upon arrival on the second afternoon following the departure of each plane from San Salvador. The average number of mosquitoes completing the trip was 8 per cent of the number put aboard at San Salvador. The average number of mosquitoes liberated in these stained batches was 70. The number captured at Brownsville on the planes ranged from one to 27, the average being 5.8 per plane. A brief description of this flight will be of interest. These are Ford Trimotor cabin passenger planes. They leave San Salvador Saturdays and Tuesdays at 7 A.M., and spend the first night in the hangar at Mexico City, with intermediary stops at Guatemala, Tapachula, San Jeronimo and Vera Cruz. On the second morning the plane takes off from Mexico City at 8-15 and arrives at Brownsville, Texas, at 12-55 P.M., with one intermediary landing at Tampico. The time consumed on the trip from San Salvador to Brownsville, Texas, is twenty-nine hours and fifty-five minutes. There are six intermediary landings, one of which is an over-night stop. The average maximum elevation reached on these trips is 14,000 feet, or more than 4,200 metres, proving that mosquitoes (*Aedes aegypti* at least) are not killed by such elevations. This elevation is one and three-fourths times greater than was reported in the Belgian experiments in sending mosquitoes in cages by air, in which it was thought high mortality was probably due to elevation.

At San Salvador we also liberated batches of stained *Aedes aegypti* on planes making trips to Miami, with a number of intermediate stops. On some of these flights the individual plane does not come all the way through. However, one plane on 8th June, 1932, left San Salvador at 7 A.M., made 10 landings and three over-night stops, arriving at Miami on the fourth day. Seventy stained specimens of *Aedes aegypti* were liberated in the plane at San Salvador just before leaving. They were put in the passenger cabin, in the cockpit and baggage compartments. Four of the stained specimens were recovered alive upon arrival at Miami. All were stained, all were gorged with blood and were from five to twelve days old. To date this is the longest time on record during which mosquitoes (*Aedes aegypti*) have been known to remain aboard an airplane on a trip seventy-nine hours and forty-five minutes in a flight from San Salvador, El Salvador, C. A., to Miami, Florida, with 10 intermediate landings, three of them over-night stops. The maximum elevation on this flight was 5,000 feet (1,524 metres) over Guatemala.

Between 28th June and 14th October, 1932, 15 cabin passenger planes on this route have been 'loaded' with stained *Aedes aegypti* at Cristobal (a few *Culex quinquefasciatus* have unavoidably been mixed with the mosquitoes stained). Approximately 840 mosquitoes were liberated on the fifteen planes, or an average of 56 mosquitoes per plane. Of the total number put aboard in the various compartments (mostly in the passenger cabin) 82 specimens, or approximately 10 per cent, were recaptured upon arrival at Miami. It should

be mentioned here that on several of these trips mosquitoes became so troublesome, especially to pilots, that an insecticidal spray was used in planes to kill the insects. Practically all mosquitoes were killed by the spraying. On one ship it was learned that a negro watchman, guarding the mail on board in the over-night stop at Kingston, 'was so troubled by mosquitoes' that he used the usual spray to kill the mosquitoes aboard. Contrasted with the results at end of trips on which it was known, or strongly suspected, that an insecticidal spray had been employed, was the ship that left Cristobal on the morning of 8th August. On 7th August, strict orders were issued from the office of the manager of operations that airplanes should not be sprayed to destroy the mosquitoes put aboard in the experiments being conducted by the United States Public Health Service. This plane arrived in Miami on the afternoon of 9th August—thirty-three hours and forty-eight minutes after leaving Cristobal, with a landing at Barranquilla, Columbia (S. A.), an over-night stop at Kingston, Jamaica, and a stop at Cienfuegos, Cuba—with 21 (35 per cent) of the 60 mosquitoes liberated on the ship at Cristobal. The maximum elevation reached on this flight is from 7,000 to 7,500 feet (2,134 to 2,287 metres).

Thirty Trimotor Ford passenger planes on regular flights between Cristobal, C. Z., and Brownsville, Texas, from 28th June to 11th October, 1932, carried a total of 1,610 stained mosquitoes, or an average of 54 mosquitoes per plane, on leaving Cristobal. Approximately two and a half days are required on this flight. The first night is spent at San Salvador, the second night at Mexico City, and Brownsville is reached at 12-55 on the afternoon of the third day—54 hours and 44 minutes after leaving Cristobal. As will be noted below, the percentage of mosquitoes recovered at the end of these flights falls far short of that on the Cristobal-Miami ships. The results more nearly compared with those on the latter route when planes are known, or suspected, to have been sprayed *en route*. Only 32 (2 per cent) of the 1,610 specimens put aboard at Cristobal were captured at Brownsville. No mosquitoes were caught on fifteen of these planes, while on the other fifteen the number recovered ranged from a single mosquito on each of six planes to a maximum of seven on one plane. It is probable that there was more routine spraying of these planes with an insecticide than occurred on the Cristobal-Miami planes.

In the series of experiments wherein stained specimens of *Aedes aegypti* were liberated on planes at San Salvador, C. A., and Cristobal, C. Z., between 4th May and 13th October, 1932, all specimens were developed from the larval stage, kept in cloth-screened cages, and allowed to feed on raisins and blood (for the females) from the arm of laboratory workers. Upon examining the recaptured mosquitoes at the end of trips note was made of gorged and ungorged specimens. A large majority of the female specimens recovered had partaken of blood meals. The ten specimens (all female *Aedes aegypti*) caught on Ford Trimotor plane No. NC 9688, leaving San Salvador on 12th June and arriving at Brownsville, Texas, after a flight of 30 hours and 55 minutes, with six landings and an over-night stop at Mexico City, were all blood engorged and well stained. As public health officials we are especially concerned with the transportation of mosquitoes that may be infected or infective. Since a large majority of the female mosquitoes used in these experiments had taken blood at least once, and in the above-mentioned experiment had taken blood fifteen or more days before, it is a safe conclusion that infected, or infective, *Aedes aegypti* may be carried from one country to another on flights of two days or longer.

It is thus shown that the known yellow fever and dengue vector of the Western Hemisphere may be carried with facility on airplanes from and to countries in which there were formerly endemic or epidemic centres. Comprehensive, but not too rigid, or unreasonable, sanitary regulations will be required in

the face of threatened introduction, through (1) proper surveillance of passengers and crews of aircraft coming from infected localities, (2) anti-mosquito sanitation at airports and their environs, and (3) proper precaution to prevent mosquito harbourage in aircraft and the destruction of mosquitoes on aircraft upon, or after, leaving airports. The same may be held true for other diseases transmitted by insects. The writer has observed house flies, honey bees and cockroaches on planes. In one experiment in the destruction of mosquitoes liberated on a Commodore passenger plane at San Juan, by the use of 'Zyklon B', in addition to the killing of all mosquitoes, the writer observed hundreds (estimated at 1,000) of cockroaches killed by the same exposure to the gas. The danger from rats and fleas carried in planes is not known. Rat droppings have been observed in airplanes, but the writer has no knowledge of rats having been found on planes.

In this brief paper some of the aspects of public health in relation to air traffic have been set forth. As stated in the original report on this subject, previously referred to: 'notwithstanding the fact that airplanes may, or do, transport mosquitoes, this mode of introduction of mosquito-borne disease' or any other insect-borne disease—'is probably secondary in importance to the importation of infected man', and 'while there is a recognized potential danger, there is no obstacle to the efficient treatment of airplanes so as to destroy mosquitoes and avoid retardation of air traffic progress'.

Calcium Thiosulphate in the Treatment of the Complications of '914' and Bismuth Administration in Syphilis

By A. E. W. MCLACHLAN, M.B.

(Abstracted from the *British Medical Journal*, 27th May, 1933, p. 916)

CALCIUM THIOSULPHATE was quite recently introduced into the therapy of post-arsenobenzol complications; it has been found especially effective in arsenical dermatitis. Sodium thiosulphate has been in regular use for this purpose for a dozen years or so, and for a much longer period calcium chloride has been used in cutaneous inflammatory conditions; theoretically, therefore, the combination of these two substances promises to be successful. The following cases of intolerance following either '914' or bismuth are recorded by the worker from his recent experiences:

(1) *Early arsenical dermatitis*.—Male, aged 31. Sero-negative primary syphilis. Developed arsenical erythematous dermatitis three weeks after completion of first course of '914' and bismuth. Calcium thiosulphate, 0.6 gramme intravenously, daily for three days, then at three-day intervals. Skin lesions completely clear on the thirteenth day.

(2) *Post-arsenical dermatitis*.—Male, aged 50. Persistent sero-positive syphilis. Developed exfoliative dermatitis, which was treated over a period of several months with sodium thiosulphate. Condition became stationary, with scattered areas of scaly, fissured, infiltrated skin over flexures of arms, legs and trunk. After twenty-two injections of calcium thiosulphate, at three-day intervals, the skin was completely clear.

(3) *Jaundice*.—Male, aged 49. Persistent sero-positive syphilis. Had post-arsenical jaundice in April 1932, which yielded after one month's treatment with sodium thiosulphate. Four months later treatment of '914' was recommenced.

December 1932, while under dual therapy. Calcium thiosulphate, 0.6 gramme intravenously, the first two doses on successive days, then at two-day intervals. Icterus completely clear after the fifth dose.

(4) *Immediate reaction (vomiting) after '914'*.—Male, aged 40. Persistent sero-positive syphilis. Vomited after each injection of '914'. No other signs of intolerance over a long period of treatment. Vomiting controlled by admixture of sodium thiosulphate; equally well controlled by calcium thiosulphate. Other

factors—bulk of injection, rate of administration, etc.—were kept as far as possible unchanged.

(5) *Bismuth dermatitis*.—Male, aged 49. Persistent sero-positive syphilis. Developed arsenical erythema while under dual therapy. This yielded rapidly to sodium thiosulphate. Bismuth administration recommenced two months later. After a course of 3 grammes metallic bismuth in ten weeks he reported with a scattered papulo-squamous erythematous rash on the trunk, with moist, fissured, eczematous lesions of serotum. The skin lesions partly cleared under the administration of sodium thiosulphate, but those of the serotum remained unaltered after bi-weekly treatment for one month. Calcium thiosulphate was then commenced. 0.6 gramme bi-weekly; the serotal lesions and the residua on the skin cleared up completely after five injections. That bismuth was an aetiological factor in the production of this dermatitis, in a skin previously damaged by an arsenical erythema, was proved by the recurrence of a similar rash on the re-exhibition of bismuth.

(6) *Dermatitis, probably due to bismuth*.—Male, aged 27. Sero-negative syphilis. Treated originally with '914' and mercury, then with '914' and bismuth. No '914' for three and a half months, during the last ten weeks of which he received 3 grammes metallic bismuth. In the eighth week of the bismuth therapy he reported a papulo-squamous erythematous dermatitis, which was aggravated by the subsequent injections. There had been no intolerance while under dual therapy, a total of 13.35 grammes '914' and 8.7 grammes bismuth having been administered. The dermatitis was considered to be due to bismuth, and treatment with calcium thiosulphate was instituted. After the seventh injection (0.6 gramme bi-weekly) the skin had completely cleared.

In one case of bismuth stomatitis the pain and discomfort were relieved by the administration of calcium thiosulphate, although clinically there was no improvement in the condition of the mouth. One case of seborrhœic dermatitis, which showed a tendency to flare up during the administration of bismuth, was markedly improved.

Apart from the feeling of intense heat in the skin, which comes on during or immediately after the injection, and persists only a few moments, the intravenous injection of calcium thiosulphate has been uneventful. Where it was possible 0.6 gramme was administered daily for three days, then injections were given twice weekly. Where sodium thiosulphate was given the first injection was 0.6 gramme, and subsequent injections 1 gramme.

CONCLUSIONS

The results of the calcium thiosulphate treatment of six cases of intolerance to '914' or bismuth are reported; in these cases calcium thiosulphate appeared to exert a definite curative influence.

Common Fungus Infections of the Skin

By C. HOWARD WHITTLE, M.A., M.D. (Cantab.)
M.R.C.P. (Lond.)

(Abstracted from *The Medical Press and Circular Supplement*, No. II, 5th April, 1933, p. xiii)

RINGWORM OF THE SCALP

It is well known that ringworm of the scalp is confined to children, and tends to disappear spontaneously at puberty, even in a case that remains untreated. The disease, which is highly infectious, starts as a circumscribed patch of scurf in which broken hairs appear early. Whitfield maintains that any marked scurfiness in a child's head should be regarded as ringworm until the most careful search and microscopic examination has proved it to be otherwise. This axiom is well worth remembering. Infected hair stumps can often be detected more readily if a little chloroform is dabbed on the patch; this causing them to appear

granular and 'frosted'. Broken hairs should be sought for, and if found the diagnosis can be established by microscoping in liq. potasse, in which they should be soaked for ten minutes. The spores are readily visible as a mosaic of round, highly refractile bodies, regular in size and structure, and situated in and around the hair. The only bodies likely to cause confusion under the microscope are red blood corpuscles and oil globules. The former are present in scanty numbers unless violence has been used in removing hairs, and should offer little difficulty: they are much less refractile than the spores. Oil globules, on the other hand, may be numerous, but vary very greatly in size, from tiny particles up to large droplets. For those who have not the time or the facilities for microscopy, a suspicious case is best sent to a dermatologist, since treatment will have to be carried out by a specialist in most cases.

While dealing with the subject of diagnosis there are two points I would stress. Confusion may arise between a patch of dandruff or psoriasis and ringworm, and between alopecia areata and ringworm. In dandruff and psoriasis there are no broken hairs, and in alopecia areata the broken hairs are typically shaped like an exclamation mark (!), and do not show the corrugated frosted appearance of ringworm hairs when treated with chloroform, neither do they contain spores. Difficulty most often occurs when the bald patch is scurfy. The differentiation is important, since complete epilation as a cure for alopecia areata is hardly the treatment one would choose. Whereas for ringworm it is the only really reliable measure. The point is not one of mere academic interest. I have had several cases of alopecia in children sent to me as ringworm for epilation.

There is one form of ringworm of the scalp, 'black dot' ringworm, which is very apt to be mistaken for alopecia areata, but as it is rare the difficulty does not often arise. In this form the bald patch is not scaly, but the hair follicles are not empty as in alopecia, and contain the remains of a hair broken off very short, and usually black in colour. This hair contains the fungus: a large-spored endothrix, not the microsporon.

The other point in diagnosis which I wish to stress is the immense help afforded by the use of a blue filter on an ultra-violet light lamp for showing up hairs infected with ringworm. In this light the hairs fluoresce brilliantly. I have been able to track down a carrier of ringworm in a school by this means when other measures and methods of examination had failed; and while epilation is taking place, it is my practice now to examine the cases each week to see that all the infected hairs fall. Even a single infected hair can be detected in a head of hair otherwise healthy. A number of clinics now use the lamp as a routine. Diagnosis is certain, and is made with great rapidity.

A form of scalp ringworm in which these filtered ultra-violet rays are not, however, of much service in diagnosis is the boggy, indolent pustular swelling known as kerion. This is commonly an inch or so in diameter, purple in colour, with pus exuding from deep indentations—the hair follicles—the hair itself being usually absent. The inexperienced may be strongly tempted to put a knife into this in order to release pus from what in some ways appears to be an abscess. But the pus is not free, and incision will be useless; moreover, the swelling and inflammation are the natural means of cure, and no treatment is as a rule needed beyond encouragement with 1–4,000 perchloride of mercury compresses.

For the forms of ringworm of the scalp other than kerion, dermatologists are agreed that x-rays are the most certain and most rapid means of producing epilation, which is essential before the disease can be eradicated. Other methods of epilation, with the exception of thallium acetate by the mouth, are, in Whitfield's words, 'dirty, painful and tedious', and if they are to succeed, require special skill in their carrying out.

Nowadays, with the aid of the filtered ultra-violet light, it is possible to define accurately the extent of

the disease, and epilatory doses of x-rays can therefore with safety be limited to the affected parts provided the case is followed up and watched for two months. I believe in the efficacy of applying an anti-parasitic ointment during the fall until all the hairs have fallen: it prevents loose fragments of hair falling about on to clothes, etc., and inhibits the growth of fungus on the scalp surface. During the fall, white cotton caps should, however, be worn in addition, and washed every other day. The ointment I use is Whitfield's:

Acidi benzoici	gr. 25
Acidi salicylici	gr. 15
Paraffini molliis	dr. 2
Oleum cocois nucifer. ad.	oz. 1

With regard to thallium acetate, many workers have used it and found it efficacious in many series of cases. I was unfortunate in my first trial of this drug, since the child was certainly not well during the fall, going off its food and looking pale and wan. I have employed it in a few cases since, and always with success. (It is given in a single dose, and the amount given is in strict proportion to the child's weight.) The indications are in those cases where x-rays cannot be given owing to the early age of the child (under four or thereabouts), or where for other reasons the child cannot be induced to keep still during the epilatory dose. In spite of these successes, I dislike using the drug owing to its undoubtedly poisonous nature.

RINGWORM OF THE GLABROUS SKIN

The difficulty in eradicating scalp ringworm depends upon the position of the fungus within the hair follicle and shaft. Drugs will not reach the spot in sufficient strength to kill the fungus without seriously damaging the skin. When ringworm occurs on the open skin the problem is usually a much simpler one.

Clinically, there are four chief forms of ringworm met with on the skin. The first, *trinea circinata*, is a microsporon ringworm which occurs on the skin of children who are, almost without exception, the subjects of scalp ringworm. The rings are pinkish in colour, slightly raised and finely scaly, are usually not more than an inch in diameter, and occur on the neck, shoulders, face, and sometimes on the arms. The scales contain the fungus. There is a large form somewhat similar, but which is not caused by the microsporon, and occurs independently of scalp ringworm; this is less common.

Another form which is seen quite commonly in agricultural communities, and which is the predominant form seen in the out-patient department in this district, is the rather heaped-up, indolent, oedematous circular patch which occurs on the face, neck, arms and hands of workers who tend cattle. This, by its firm, raised, indolent, usually painless character, often suggests an infective granuloma such as a gumma, or even in some cases actinomycosis. Usually it is possible to trace the follicular origin, and pus that may be expressed comes from the lanugo follicles. In this or the lanugo hair it is possible to find the fungus, a large-spored type, of which the spores are oblong, and are usually arranged in chains. The diagnosis is easily made once the possibility has entered the mind of the practitioner, and those practising in agricultural districts soon acquire a familiarity with it. A history of association with cattle gives the clue. I have occasionally seen this form on the arms and legs of children, and it is possible that infection takes origin from fences and gates on which the children play, and on which cattle may frequently be seen rubbing themselves; at least this seems to me a likely explanation in the absence of a history of direct contact with infected animals.

A third important form which has been much more prevalent since the War is *trinea cruris*, or dhobi's itch. This form occurring in the groin and perineum as sharply marginate, scaly, itchy erythematous patches is also common in Cambridge, but for quite another reason. It appears in undergraduates, who usually bring

it with them from the public schools. It is a highly contagious disease, and often spreads widely in schools. Clothing, towels and baths are probably the means of spread, and boys are apt to be careless in these matters. It is not, however, confined to boys and young men, but may occur in persons of all ages. I recently saw a case in a lady, eighty years of age, which had puzzled her doctor for some weeks. Infection in such a case is possibly *via* a lavatory seat.

The older name for this form was *eczema marginatum*. It may present a raw, weeping surface, instead of the more common, dry scaly characters, but the important feature leading to a diagnosis is the sharply defined marginate nature of the lesion. It may be several inches in diameter. The scales show an abundance of the fungus in the form of a long, branching, fairly stout, mycelium. Liq. potassæ preparations show it well.

A fourth form caused by the same organism is the intertriginous ringworm found between the toes, causing a sodden, reddened, scaly, sharply marginate lesion running a slow and chronic course. This form also appears to be increasing in frequency, and in America investigations indicate that spread is from person to person in the footways of swimming baths. This type usually affects the cleft between the little toe and the next, and may spread to adjacent clefts and involve the distal part of the foot, both dorsum and sole. It frequently remains localized to one foot, and this feature, when present, is in favour of the diagnosis, and against a non-infective eruption. The mycelium can usually be found without much difficulty in the scales. The same fungus may cause a vesicular eruption of the hands not unlike cheilopompholyx. The fungus can be demonstrated in the roofs of the vesicles.

The occurrence of generalized eruptions, secondary to the local affection, and known as trichophytides or epidermophytides, has been noted in recent years. One form very like lichen spinulosum occasionally occurs in connection with epidermophytosis of the feet. An undergraduate came to me for the treatment of a patch of horny follicular spines appearing on the extensor aspect of the forearms, and it was not until I made special inquiry that I discovered a lesion of the toe clefts, which examination proved to be due to ringworm. The treatment of the latter undoubtedly played a part in clearing up the trouble on the arms.

The treatment of body ringworm is simple, and most lesions clear up in a week or so under either 1-4,000 mercury perchloride compresses, which are specially suited to the heaped-up cattle types, or Whitfield's ointment for most of the others. Toe ringworm may require double strength ointment, and it is important to clip away the frayed scaly edges, and keep the toes separated. More resistant cases of toe ringworm will respond to 1-2,000 warm baths of potassium permanganate twice daily (Whitfield). Ultra-violet light is cumbersome, and usually unnecessary for treating body ringworm. Simpler methods are to be preferred.

RINGWORM OF THE BEARD

This commonly manifests itself as a circumscribed boggy patch on one side of the face, with some pustulation in the follicles. The fungus, which is a large-spored type, can be found in the pus or hair stumps. The differential diagnosis from syecosis of staphylococcal origin presents certain difficulties. The latter is less heaped up, less boggy, and less frankly pustular, and runs a more chronic course. Usually beard ringworm will yield to mercury perchloride compresses. X-ray treatment will cause resolution in resistant cases.

RINGWORM OF THE NAILS

One or more nails on one hand may be affected, and the nail is much coarsened, longitudinally ridged and thickened. Scrapings must be soaked twenty-four hours in potash before the fungus is visible under the microscope. X-ray treatment offers the most rapid method of cure, but some cases may be very resistant to treatment.

TINEA VERSICOLOR

This condition shows as a yellowish-brown discoloration of the skin, usually the trunk, with a sharply defined edge. It may extend in a sheet across the trunk, or may occur in patches only. The lesion is not visibly or palpably raised, and may not even be scaly.

I have had patients referred as cases of Addison's disease on account of the pigmentation, but the discoloration is all on the surface of the epidermis, and, if the horny layer is scraped off, the fungus *Microsporon furfur*, is found in abundance as mycelium, club-shaped bodies, and spores. The condition is not very infectious, as a man may have it for years and not give it to his wife. It clears up readily with Whitfield's ointment.

Observations on the Cure of Malaria with Atebrin

By A. L. HOOPS, C.B.E., M.D., N.P.H.

(Abstracted from the *British Medical Journal*, 10th June, 1933, p. 993)

THE PROBLEM IN MALACCA

THE population with which my colleagues and I deal consists of over 19,000 rubber estate labourers and dependents, and of the staff—European and Asiatic—with their households, numbering over 800, who control the estates.

TREATMENT OF MALARIA WITH ATEBRIN

For the actual treatment of malaria reliance has hitherto been placed on that old and tried remedy quinine. On European estates the sufferer from primary malaria has received full doses in hospital for perhaps ten days, followed by smaller doses, for perhaps three weeks, in the lines. He has been given more quinine when at labour inspections he has been found to possess an enlarged spleen. And yet, with all this dosing, it is well known that over 50 per cent of sufferers so treated relapse and have further attacks of malaria, in some cases repeatedly, and for years after the original infection. There are several notable disadvantages attending the use of quinine such as the long continuance of the treatment, the difficulty of carrying this out, the lowering effect on the vitality of its continued administration, the great liability to relapse, and, finally, the expense.

Beginning the trial of atebrin in June 1932, I have found that it has apparently brought about a permanent cure in the great majority of 153 malaria cases treated by me between that month and the end of the year. Two of my colleagues, Dr. I. D. Stubbs and Dr. Foo Hce Seng, who started to use the drug in August 1932, have had similar results among 163 cases treated by them. Our combined figures are:

Total cases treated	TYPE OF MALARIA				Relapses
	Subtertian	Benign tertian	Quartan	Unclassified	
317	98	114	5	100	11

Eighteen of the ninety-eight patients under the heading 'subtertian' were cases of mixed infection, showing benign tertian parasites as well. In four subtertian cases, in which cerebral symptoms appeared, I administered from two to six doses of quinine bihydrochloride intramuscularly, with one death. The 'unclassified' patients were mainly on estates where no microscope was available, but were clinically cases of malaria. The figures for relapse up to the end of March 1933—that

is, over nine months after the first case and three months after the last case was treated—are eleven. The relapses usually occurred within two months of the first treatment, the types of malaria in which these were noted being subtertian (three), benign tertian (two), unclassified (six).

Relapse rate

There is little movement among labour forces at present, and it has therefore been possible to keep in touch with the great majority of those treated. Deducting, however, the liberal allowance of 20 per cent from the total 317 patients treated, on account of persons since lost sight of, there remain 253 treated and still under observation, with eleven relapses—a relapse rate of 4.34 per cent. All persons once treated with atebrin and having further malarial attacks have been counted as relapses, though some may have been fresh infections. Of the eighteen cases of mixed infection, eleven occurred on one division, where there was a violent outbreak of malaria due to a temporary failure in oiling—thirty-eight out of a population of sixty-seven being affected within one month. Microscopical findings were: fourteen subtertian (of whom eleven showed benign tertian parasites also) and twenty-four benign tertian. In spite of so many double infections, there has not been a single relapse on this division, though seven months have passed since treatment was given.

Death rates

A comparison of the labour death rates among those treated in hospital with quinine and with atebrin respectively is of interest. In 1931, 934 cases of malaria were treated in hospital, all with quinine: 10 grains of the sulphate or bihydrochloride were given in solution three times daily for nine or ten days, followed usually by small doses of quinine in the lines for three weeks. Deaths numbered thirty-one; death rate, 3.31 per cent. In 1932, 288 patients were treated in hospital with quinine, of whom fourteen died; death rate, 4.85 per cent. Of the 317 patients who received atebrin, 257 were treated in hospital, with four deaths—a death rate of 1.55 per cent. Both the relapse rate and the mortality rate, therefore, favour atebrin treatment. Of the labour population, averaging 19,511 last year, two-thirds were Southern Indians—mostly Tamils—less than one-third were Chinese, and about 1,200 were Malays; 55 per cent of those treated with atebrin were Tamils.

Staff treated

In addition to labour, eight Europeans, including two ladies, and ten members of the Asiatic staff were treated for malaria with atebrin in the last half of the year 1932. All found it easy to take, and experienced a sense of well-being after it. None has so far relapsed.

Particulars of treatment

A course of atebrin lasts as a rule for five days only. The daily amount administered is 0.3 gram (4½ grains) for adults and for children over 11, 0.1 to 0.2 gram (1½ to 3 grains) for children of 5 to 10 years, and 0.035 to 0.1 gram (½ to 1½ grains) for children of 1 to 4 years, and is given in three divided doses. In addition, plasmoquine is prescribed in subtertian cases only, also for five days—0.03 gram (½ grain) daily for adults in three divided doses; children of 11 receive only half this dose of plasmoquine, and younger children proportionately less. The bowels are kept freely open throughout. The tablets of atebrin and plasmoquine are crushed and taken with a drink of water half an hour before meals. Most patients are also dosed with oil of chenopodium to remove their ankylostomes, and those who need it have santonin to relieve them of round-worms. At the conclusion of the treatment patients are placed on an iron and arsenic tonic. No quinine has been given with atebrin by me, except by injection in a few severe cases.

ADVANTAGES OF ATEBRIN

The points in favour of the use of atebtrin in place of quinine are:

(1) The fever is usually reduced as quickly as with quinine; it is uncommon to find a temperature above 99°F. after forty-eight hours' treatment. In two cases only did fever persist as long as the fifth day; for these atebtrin was continued for eight days.

(2) With the exception of subtertian gametocytes, it is rare to find malarial parasites in the blood after the second day of treatment. No parasites of any description were found in the blood of any hospital case on the conclusion of treatment.

(3) The treatment is short, simple, and effective—one 1½-grain tablet three times a day for five days only, as against a prolonged course of quinine.

(4) The drug is not unpleasant to take, and is not depressing. It is well tolerated, even by pregnant women and young children and in blackwater fever, and also by persons suffering as well from other diseases such as pneumonia and influenza.

(5) Relapses are rare after atebtrin, while with quinine the relapse rate is high.

(6) The cost of a course of atebtrin (fifteen tablets) is about 75 cents (1s. 9d.), that is, less than the cost of a course of quinine—one ounce, about \$1 (2s. 4d.)—not to speak of the cost of treating the frequent relapses when quinine is used.

(7) In malaria of the benign tertian and quartan types atebtrin only is necessary.

(8) When malaria is subtertian in type it is necessary to give a five-days' course of plasmoquine in addition to atebtrin (cost about 43 cents, 1s.), but this is also needed when quinine is employed, as subtertian gametocytes are unaffected by either quinine or atebtrin.

(9) Last, but not least, atebtrin is a powerful preventive of malaria in the sense that most of those treated with it, being cured, are rid of the infection and completely non-infective to their fellows. It may well prove that the regular use of atebtrin—plus plasmoquine in subtertian cases—for the cure of malaria will lessen the amount spent on antimalarial drainage and oiling.

LIMITATIONS OF ATEBRIN

Are there any serious disadvantages in the use of atebtrin? So far as my experience goes, 'No'. A few patients have colicky pains about the last day of treatment, and a few show a temporary yellow discoloration of the skin and conjunctiva, due not to jaundice, but to the fact that atebtrin contains a yellow dye. No form of the drug suitable for injection is yet available; consequently, in very severe cases of malaria, it is advisable to administer one or several doses of quinine, generally by intramuscular injection. Some medical men, though now using atebtrin for malaria, are prescribing quinine during the first two days of treatment. This may be quite sound, but personally I have as far as possible employed atebtrin alone in order to test fully the value of that drug without quinine.

In a progress report issued locally in November 1932, R. Green states that both benign tertian and quartan parasites, including gametocytes, disappear from the blood more quickly with atebtrin than with quinine. In subtertian malaria the rings disappear either with quinine or with atebtrin in about three days. The febrile period in all types is slightly shorter with atebtrin than with quinine, but, pending the cessation of febrile symptoms, the temperature among some of the subtertian cases seems to remain on the whole somewhat higher, and the patient to be more prostrate, than with quinine. The subtertian infection varies from the very mild case to the fulminating case, attended with fatal results whatever the form of therapy. In the small but certain proportion of subtertian cases which show alarming symptoms, Green regards it as at present advisable to administer quinine for two or three days as a preliminary to atebtrin.

Green's relapse rates

Among forty-three patients who had 30 grains of quinine bishydrochloride a day for seven days, and were under observation for a maximum of forty-six days, Green's record is:

	Total cases	Relapses
Benign tertian	.. 12	6
Subtertian	.. 13	5
Quartan	.. 18	5

Among forty-eight cases receiving a six-days' course of atebtrin, and kept under observation for a maximum of eighty days (seventeen being benign tertian, twenty-three subtertian, and eight quartan), Green observed one relapse—a benign tertian case on the thirty-second day after treatment.

CONCLUSION

The treatment of malaria with atebtrin is short, simple, and economical. Most sufferers appear to be cured within a week. The consistent use of this drug should effect a great and permanent diminution of malaria among labour forces by sterilizing most of the reservoirs of infection.

The Use of Digitalis other than in the Treatment of Cardiac Decompensation

By HENRY A. CHRISTIAN, M.D.

(Abstracted from the *Journal of the American Medical Association*, 18th March, 1933, Vol. C, No. 11, p. 789)

CARDIAC HYPERTROPHY, instead of being a beneficent process, is an injurious influence on cardiac function; the heart, once enlarged, is already on its way to eventual decompensation: to retard hypertrophy is to prolong cardiac efficiency.

Clinical observation has taught that with few exceptions the enlarged heart rarely recedes in size and that sooner or later the enlarged heart shows signs of inefficiency. It may be taken as a clinical dictum that cardiac hypertrophy with rare exception is the first evidence of cardiac failure, though it may long antedate any symptoms or signs of cardiac insufficiency. If one considers that type of heart disease which is most frequent in adults, so-called chronic myocarditis, chronic non-valvular heart disease or chronic myocardial insufficiency, whatever term one prefers to use for this condition, it will be found that the foregoing statement is unqualifiedly true.

If, then, as I believe, cardiac enlargement is functionally harmful, intelligent therapeutics will seek to retard it. It is generally believed that increased demand on cardiac function serves to increase cardiac enlargement, and so clinicians advise patients with enlarged hearts to decrease their physical exertion. Can anything else be done in the way of treatment? I believe that just here digitalis has a definitely desirable effect, and if given daily in moderate dosage it will retard cardiac enlargement and delay the appearance of symptoms and signs of cardiac insufficiency. Consequently I advise patients in whom I find enlargement of the heart to decrease physical exertion and to take continuously from 0.1 to 0.15 gm. of digitalis leaves twice daily, unless this amount causes toxic symptoms, as occasionally it does. If that happens, the dose is reduced to a point at which no toxic symptoms appear. Digitalis for these patients is continued throughout the remainder of life. The optimum dose is that just below the one which eventually produces toxic manifestations, a dose to be determined by the method of trial and error.

USE OF DIGITALIS

If cardiac insufficiency has developed to a point to produce symptoms and signs marked enough to interfere with the individual comfort and activities, it is said that cardiac insufficiency has developed or that the heart is decompensated. Rest and digitalis is the

practically universally instigated therapeutic management of such cases. In a large percentage so treated, symptoms and signs of cardiac insufficiency very largely disappear. With return to a greater degree of physical activity, sooner or later a return of the same symptoms and signs is to be expected. Clinical experience indicates that, if to such patients a daily ration of digitalis, short of toxic effects, is given, this return of evidences of cardiac insufficiency will be delayed. Consequently it has become a quite general practice to give such patients digitalis continuously in amount just short of toxicity, the proper amount approximating 0.15 to 0.25 gm. daily of powdered digitalis leaves, the exact amount being determined by the method of trial and error, some patients tolerating more and others less than this daily ration in the sense of being just short of toxicity. This elsewhere I have termed the continuation treatment with digitalis.

Now if digitalis, thus used as a continuation treatment, is helpful under the circumstances just enumerated, it is reasonable to suppose that, if given in this way prior to the development of symptoms and signs of cardiac insufficiency, development of these symptoms and signs might be delayed. My own clinical experience seems to be in accord with this idea, and so I have come to give digitalis in this way to patients in whom I can detect evidences of cardiac disease, particularly cardiac enlargement. It does seem as if cardiac enlargement is retarded and that these patients are capable of greater activity without having symptoms or signs of cardiac insufficiency than are patients otherwise similar not receiving digitalis.

There are certain individuals in whom, although there is no detectable evidence of cardiac enlargement, one can feel quite certain that sooner or later enlargement of the heart will take place. The most numerous in this group are individuals with hypertension and next in frequency come those who have developed a diastolic murmur of some sort or who, with a past history of rheumatism, show a systolic murmur without any murmur in diastole. The query naturally occurs in light of what I have just been saying. Why not give digitalis to such individuals?

Certain observations of pharmacologists investigating digitalis have a bearing on this suggestion. At one time it was believed that digitalis would cause cardiac hypertrophy, but many experiments have shown that this did not occur. Cloetta noted that animals receiving digitalis over long periods of time had even lighter hearts than those receiving no digitalis. Furthermore, he found that, if aortic insufficiency was produced, animals subsequently given digitalis had hearts both smaller and more efficient than did animals with similar aortic lesions not receiving digitalis. Here is experimental evidence in favour of the clinical thesis that I have just enunciated in regard to beginning digitalis even prior to the development of hypertrophy in those patients in whom hypertrophy may be expected to develop.

Observation has shown that in the aging process the heart muscle loses water. Other observations show that one effect of digitalis is to increase hydration in heart muscle. This points to a probable therapeutic effectiveness of digitalis for elderly patients not to be expected in the young. Heart disease due to myocardial insufficiency is most frequent in the later decades of life. Clinical experience points to a particular usefulness of digitalis in just this group of individuals, those past middle life (40 to 50), with cardiac enlargement without valve lesions, not yet having symptoms or signs of cardiac decompensation. Competent observers believe further that in elderly people with no evidence of cardiac enlargement but in whom circulatory efficiency is lessening, digitalis increases heart efficiency, and here digitalis possibly may be said to have a definitely 'tonic' effect, presumably increasing the hydration, which has decreased in the aging process.

Pharmacologists have demonstrated a certain automaticity in the regulation of digitalis effects that help in the treatment of patients with cardiac enlargement.

Digitalis, before it exerts any digitalis effect, is fixed in the heart muscle. After fixation in the heart muscle it is split up into an inert carbohydrate and a substance that produces a digitalis action. This fixation varies directly with the concentration of digitalis circulated to the heart muscle and with the bulk of the heart muscle but indirectly with the rate of circulation through the muscle. These laws of digitalis action influence the effectiveness of digitalis therapy. As the heart enlarges, all other factors being unchanged, a given dose of digitalis has an increasing effectiveness in ratio to the increasing bulk of the myocardium. As the myocardium loses in efficiency, the circulatory rate in the coronary system of vessels is slowed. As a result of this, more digitalis is fixed in the heart muscle fibres and this causes an increased digitalis action. In other words, within certain limits, an automatic increase in digitalis action occurs under just those circumstances that would need a greater digitalis action and that without any increase in size of dose. As heart action improves, circulatory rate through the myocardium accelerates and fixation of digitalis decreases, thus bringing about a lessened effect from a given dosage than would be the case were there not this relationship. In other words, when there is more need for digitalis, digitalis is proportionately more effective, and when the need decreases, the same dose of digitalis has less effectiveness. This saves the clinician from the necessity of continuously changing digitalis dosage to meet changing function of the heart muscle.

VALVULAR HEART DISEASE

What has been said about non-valvular forms of heart disease applies, too, to valvular types of heart disease except that since valve lesions occur chiefly in younger people, in whom heart muscle has not lost water, the action of digitalis on heart function is less effective than when given to older persons. Also, as valve lesions introduce an unchangeable mechanical factor decreasing heart efficiency, again not so striking an improvement is to be expected from giving digitalis to these patients. However, since there is no harm caused by giving digitalis, it is reasonable to give it, too, in valvular heart disease as just advised for non-valvular heart disease both prior to and subsequent to the appearance of symptoms and signs of cardiac decompensation. It seems probable, however, that here it will not be as useful as with non-valvular forms of heart disease.

LONG CONTINUED DOSAGE

Digitalis for the conditions just being discussed is continued over very long periods of time. Obviously, if a drug is to be taken daily over long periods of time, it is essential that the drug has no harmful effects, direct or indirect, that it has no habit-forming qualities and that from continuous use it does not lose its effectiveness. There is no pharmacologic or clinical evidence that any of these things happen. Repeatedly have I seen the patient who has been taking a daily dose of digitalis for weeks and months respond to an increased dose indicated by reason of developing evidences of cardiac decompensation, in just the same way as a patient with similar evidences of cardiac failure who had received no previous digitalis therapy.

If one will stop to think of the way digitalis acts, it will be seen to be an ideal drug, pharmacologically, for long continued dosage. Digitalis given by any route or dosage reaches the heart muscle, where it is promptly fixed or bound. In a short space of time it commences to be split within the muscle into a part that has digitalis action and an inert part. This splitting is a gradual process, long continued, very slowly decreasing in the degree of digitalis action on the heart muscle. Before one dose has ceased to act, another can be given, which in its turn will be fixed and split and continue a digitalis effect. It is entirely possible on account of this way of action to space properly sized doses of digitalis so as to maintain a digitalis action throughout the twenty-four hours with but little fluctuation from hour to hour.

in the intensity of that action and to continue it practically indefinitely from day to day by suitable doses not closer together, let us say, than twelve hours. Could there be a more ideal mechanism for maintaining a therapeutic effect over very long periods of time? In this respect digitalis has a part almost like the replacement therapy of thyroid gland substance in myxœdema, insulin in diabetes mellitus and liver extract in pernicious anemia, for all of which physicians say to their patients, you must continue taking this daily so long as life lasts.

The Problem of Relapse in Chronic Pulmonary Tuberculosis

By R. C. WINGFIELD, M.B. (Oxf.), F.R.C.P. (Lond.)
(Abstracted from the *Lancet*, 3rd June, 1933, Vol. I, p. 1166)

By relapse I do not mean merely the reappearance of symptoms, but I mean the appearance, and often the sudden appearance, of definite fresh lesions in those parts of the lung where no lesion was demonstrable before. I certainly do not mean the insidious direct spread of lesions already present.

STUDY OF A PARTICULAR CASE

I have tried to make a special study of these relapses and have been fortunate enough during the last few years to have seen a good many. I am sorry to think how many I may have overlooked. Of these I propose to describe one fairly typical case which will illustrate many of the clinical features that I have learnt to associate with these relapses, and to argue as from that.

A. C., a big strong boy of 20, had a left artificial pneumothorax, induced in the Brompton Hospital, to which he made an excellent response. He was sent to Frimley and went through his sanatorium course without relapse. He was afebrile, with a normal pulse rate, had no cough or sputum, and made a good gain of weight. When ready for discharge he stayed on, doing heavy manual work on the sanatorium pig farm in return for board and artificial pneumothorax treatment.

This consisted of a full eight-hour day of heavy physical work, and he kept in splendid health without symptoms or loss of weight for one year. One day he developed a common cold in the head with all its usual symptoms and slight fever. His temperature rose to 100°F. on the first day and settled to normal by the seventh day, and I would like to point out the mildness of the pyrexia and its rapid disappearance. Also it is important to note that his symptoms were slight and, beyond the reappearance of sputum non-localizing further, that they rapidly disappeared. An x-ray was taken, although there was no marked change in physical signs. His previous film showed a collapsed left lung and a right lung clear of disease; the new film showed a dense hazy opacity the size of the palm of the hand in the right subclavicular region. In fact, a new lesion of considerable size had appeared in his right lung. He was kept on complete rest for one month, during which time all symptoms and constitutional disturbance disappeared and he seemed perfectly recovered, but since a further x-ray at the end of that time showed no clearing of the new lesion, a selective right-sided artificial pneumothorax was induced, and he has been back now at the same work for 12 months in excellent health.

Now it will be instructive to picture what would probably have happened in his case had he been fully discharged from the sanatorium, and had not been an artificial pneumothorax case, and as such under close supervision. He would have reported to his tuberculosis officer and have been found to have done well and probably advised to go back to work and to report at stated intervals. He keeps well, but one day he

gets this cold, and, as a keen hard-working boy, he would probably have ignored it altogether, or perhaps would have taken one day off work. If it had happened in between his visits to his tuberculosis officer, the latter would probably have heard nothing at all about it. The symptoms disappearing rapidly, he would carry on blissfully unconscious of this new lesion. How long? One cannot say; it may be only for a short time, but experience tells us that it may be many months before definite symptoms from this new lesion appear and cause the patient to seek medical advice. If there are some residual symptoms from the previous lesions the visit to the doctor will probably be longer delayed. Much depends on the patient's intelligence and outlook, and on the efficiency of the individual dispensary's control of its cases. But in any event it is unlikely that the tuberculosis officer will see him until this 'secondary' lesion (if I may be permitted to use my own terminology) has turned into a well-entrenched irreparable damage is done—treatment starts again—and handicapped treatment. For my experience of these 'secondaries' is that if they are caught young and energetically treated, often by rest alone, they can usually be healed. The same cannot be said of an 'intermediate'.

THE ALLERGIC REACTION

To go back to some pathological considerations. I have stated elsewhere my belief that these fresh areas of disease are due to an hematogenous deposit of tubercle bacilli in the interstitial tissue of the lung, setting up around themselves an allergic reaction of simple acute inflammation. If this is true, the x-ray shadow that appeared in this case had a small core of tuberculosis and a large capsule of simple acute inflammation which cast the main shadow. The fate of this composite lesion depends partly upon the patient's individual resistance to tuberculosis, partly on his environment or treatment, and partly on the intensity of the allergic reaction. The allergic reaction has been assumed to be beneficial; it may be so to some extent, but not entirely. In support of this I quote A. R. Rich, who has devoted so much time to the study of allergy. He says:

'The damage done by allergy in this disease is very serious indeed. A great part of the tissue destruction in tuberculosis is due to hypersensitivity to the protein of the tubercle bacillus. The prevention of this damage by means of desensitization might be of great service to many tuberculous patients. I am thoroughly aware of the virtue of inflammation as a protective mechanism. I question here only the virtue of that excessive inflammation accompanied by necrosis which characterizes the allergic reaction..... Allergy converts the comparatively harmless protein of the tubercle bacillus into a virulent poison.'

To return to our composite lesion, either the whole thing heals leaving a minimal scar, or, as the simple inflammation subsides, the tuberculous core spreads into the damaged or necrosed surrounding tissue, and we are left with an active spreading 'intermediate' lesion. I believe that the time this lesion takes before it produces symptoms depends on two factors, (1) the rate of spread, (2) the erosion of a patent bronchiole which throws the lesion open to the fauna and flora of the respiratory tract, and permits secondary pyogenic infection to complicate the pure tuberculosis. We see from day to day so many cases who can tolerate the tubercle bacillus and its lesions without symptoms and without constitutional disturbance that it seems we must postulate something of the sort to explain why some patients get all the classical symptoms and others do not. This one example from many cases that I have studied illustrates, I am certain, what happens to the great majority of those cases who do badly after routine institutional treatment when they might have done well. Incidentally, it is the story of the reasonably early case, or indeed almost any case, presenting himself for his first diagnosis.

FIVE SALIENT FEATURES OF RELAPSE

It may be well to review the position and underline the five salient features of relapses of which C's case may be taken as a fairly typical example. These five features are as follows:

- (1) These relapses have no obvious prodromata.
- (2) The new deposit may in some cases be entirely silent; in most cases the symptoms and constitutional disturbance that accompany it are so slight that they can be too easily ignored; occasionally it is accompanied by a severe reaction.
- (3) In many cases physical examination conveys but little information, and if the new deposit is accompanied by physical signs these are often evanescent.
- (4) The symptoms and constitutional disturbance are usually of very short duration and disappeared completely.
- (5) There is an indefinite latent period before the second reappearance of symptoms. And I should like to add that these again will often yield to the mildest treatment.

If it can be agreed that these relapses are a common cause of our ill-success, how shall we meet the problem? The obvious answer is to have much closer clinical and x-ray control for the critical two years after institutional treatment. For facts tell us that neither routine institutional treatment nor its adjunct collapse therapy will protect our patients with any certainty from these new lesions. But such a suggestion is rather like the tardy shutting of the stable door. For although it is true that a fresh lesion will usually respond to treatment excellently if caught early, it does necessitate further treatment. This is distressing and discouraging to the patient, often-times forcing on him mental, social, and financial hardship and imperilling his already slender chances of getting, or keeping, a wage-earning job. For the country, too, it is economically unsound. We should if possible find a means to prevent these relapses.

The sensitiveness or the allergic state of the patient gives us a clue. Allergy and immunity are two entirely different things. I think Professor Leroy Gardner has expressed this very happily when he says 'Allergy and immunity are created by the same condition—i.e., the experience of infection—but their subsequent courses are not necessarily parallel'. But since the greater part of these lesions is, I believe, a simple allergic inflammation, beneficial perhaps in some respects but at the same time an excellent hotbed for the spread of their tuberculous core, I believe that if we can render our hypersensitive patients less sensitive we shall to a great extent protect them. And in this belief I have the theoretical backing of Rich in the excerpt I quoted above.

SENSITIVENESS AND DESENSITIZATION

If this conception is correct, one reason why one patient relapses and another of the same type and under the same environment does not is because the one is more sensitive than the other. Consider these figures from the South African Institute of Medical Research (Rept. XXX, vol. 5, 1932). Of 93,979 natives presenting themselves for enrolment in the mines, 61,115 were found to be already infected by giving a positive Mantoux reaction to a 1/5000 dilution of old tuberculin. Of these, 3,879 gave a ++ response—i.e., were highly sensitive—while 57,236 gave a simple + response—i.e., were less sensitive. Among the highly sensitive the incidence of subsequent clinical tuberculosis—mostly, I think, pulmonary—was 1.03 per cent, while among the less sensitive it was a little more than half that, 0.65 per cent. I am fully prepared to have Heimbeck's experience of the nurses and students at Oslo quoted against me here, but the two situations are entirely different. Heimbeck was dealing with the problem of primary tuberculous infection and resulting clinical disease in non-infected people exposed to the bacillus for the first time. The South Africans, and we, are dealing with the problem of the likelihood of the appearance of secondary pulmonary tuberculosis, and its

subsequent relapses, in a previously infected population.

For a great number of our successfully treated cases one of the important factors in their prognosis, then, is their degree of sensitiveness. If this is high they are in greater danger than if it is low. I am fully aware that their degree of immunity is probably as, or even more, important a factor. We are, however, woefully ignorant of tuberculo-immunity, so at present we cannot attempt to influence it. But animals, and again I quote Rich as my authority, can be desensitized by tuberculin, and we know that man can be desensitized to tuberculin by tuberculin. This therefore seems the logical course to pursue.

Desensitization to large doses of tuberculin is a perfectly safe procedure if carefully controlled, and since it would entail much closer clinical control of the ex-institutional patient I can see but little argument against it. At the worst it can only be a waste of time. There are many things one would like to know. Is the degree of sensitiveness a variable quality, or is one person always hypersensitive and another always hyposensitive? If sensitiveness does vary in the individual from time to time what factors govern this variation? It is extremely interesting to find that it does vary widely in different persons, irrespective of their clinical or pathological condition at the time of making the test. If a person is desensitized, how temporary or how permanent is the loss of allergy is another important question to answer.

Along these lines an attempt is being made to prevent relapse in immediately successfully treated cases. We shall have to wait, I am afraid, at least five years, more probably ten, before results can be tabled.

Sodium Dehydrocholate in Arsphenamine Poisoning

By BERNARD APPEL, M.D.

(Abstracted from the *Archives of Dermatology and Syphilology*, March, 1933, Vol. XXVII, p. 401)

(1) ARSPHENAMINE in therapeutic doses is rapidly metabolized in the liver.

(2) After the lethal dose of arsphenamine, the liver contains a maximum amount of arsenic and is apparently the only organ of storage.

(3) One hour after a lethal dose of neoarsphenamine, all parts of the lobules of the liver are loaded with arsenic.

(4) Twenty-four hours after a lethal dose of tryparsamide, the liver begins to show degenerative changes.

Thus, most of the damage to the liver is apparently done within the first few hours after the administration of the arsenical. It seems logical to state that symptoms related to this damage could be controlled if this early storage of arsenic could be prevented. If it were possible to produce an increase in the rate of excretion of bile and to maintain this for some hours following the injection of an arsenical, this would constitute a washing-out process during which it would be difficult for arsenic to become stored.

There are two types of reaction to the arsenicals that are related to liver metabolism: one is jaundice; the other is the gastro-intestinal reaction characterized principally by nausea and vomiting. The latter may occur either immediately after the injection, occasionally even before the needle is withdrawn, or may be delayed for a number of hours. These two types of reaction are disturbing and are prominent causes of reluctant cessation of the use of arsenicals in cases in which they would otherwise be definitely indicated.

In a study by Stokes and others, of 3,244 patients with syphilis treated with arsphenamine, gastro-intestinal reactions developed in 7.49 per cent and jaundice in 2.34 per cent.

Pertusal of the current literature disclosed work in Europe along the line of prevention of these reactions with sodium dehydrocholate.

Dehydrocholic acid was developed in 1881 by Hammarsten and introduced for clinical use by Neubauer in 1923. It is an oxidation product of cholic acid, one of the bile acids. The sodium salt is freely soluble in water, is weakly alkaline in reaction and has a bitter taste. It differs principally from cholic acid in being practically non-toxic. The salts of taurocholic and glycocholic acids have a degree of toxicity which precludes them from intravenous use.

Administered intravenously, sodium dehydrocholate causes definite increase in the quantity of bile excreted. This effect is most marked within the first thirty minutes after injection and continues for a total of about ninety minutes. The only known contraindication to its use is absence of bile in the stools.

C. Costinescu, of Bucharest, treated seventy-six syphilitic patients with large doses of arsphenamine (15 mg. per kilogram of body weight) by mixing the arsphenamine solution with 5 c.cm. of 20 per cent solution of sodium dehydrocholate before injection, without encountering toxic reactions.

A. Șavulesco also reported a number of cases in which the patients were treated with very large doses of arsphenamine mixed with a solution of sodium dehydrocholate. He concluded, among other observations, that sodium dehydrocholate decreases the toxicity of the arsphenamine.

Hans Abelsolm reported the cases of seven patients in whom jaundice developed during the course of injections with neoarsphenamine, but whose treatment was successfully continued by mixing the subsequent injections with sodium dehydrocholate solution. He stated that this solution should be given in cases of jaundice whether the condition is due to syphilitic involvement of the liver or to arsenical poisoning.

In the five cases of jaundice and in the case of gastrointestinal reaction herewith reported, the patients were treated with sodium dehydrocholate administered intravenously. The patients were all being treated for syphilis in the out-patient department; they had all received varying amounts of neoarsphenamine intravenously.

REPORT OF CASES

Case 1.—A white man, aged 69, married, was admitted to the hospital on 1st April, 1932. Jaundice developed while he was being treated with neoarsphenamine. On admission he was given an intravenous injection of sodium thiosulphate as the use of sodium dehydrocholate had not been instituted at that time, and on 8th April, intravenous injections of the latter were begun. The patient received a total of 105 c.cm. in eleven injections.

On 6th May, the patient was discharged to the out-patient department feeling well but with a mild residual jaundice. One noteworthy effect of the treatment was a marked increase in appetite. This occurred in almost every other case of jaundice in which similar treatment was given.

Case 2.—A white man, aged 24, single, was admitted to the hospital on 31st March, 1932. He had previously been in the hospital from 12th March to 24th March, 1932, because of arsphenamine hepatitis. An infection of the upper respiratory tract had developed, which was still present; a recurrence of jaundice was also noted. Treatment was started with one intravenous injection of sodium thiosulphate and dextrose, but a week later injections of sodium dehydrocholate were begun.

The patient was discharged to the out-patient department on 6th May feeling well and symptom-free, except for a slight residual jaundice.

Case 3.—A white man, aged 52, married, was admitted to the hospital on 2nd April, 1932. He had been treated with neoarsphenamine, and jaundice had developed. He was given one intravenous injection of sodium thiosulphate at entry. Soon after this, injections of sodium dehydrocholate were started. While in the hospital, the patient complained of vague abdominal and peripheral

pains, which were considered to be related to the syphilitic involvement of the central nervous system. The Wassermann test of the spinal fluid was positive, as was also that of the blood.

He was then transferred to a state institution for further antisyphilitic treatment, the jaundice having improved markedly.

Case 4.—A white man, aged 44, single, was admitted to the hospital on 14th April, 1932. He had been treated with neoarsphenamine in the out-patient department for syphilis. Jaundice had developed, and before admission he had received several intravenous injections of sodium thiosulphate.

Although still somewhat jaundiced, the patient was discharged at his own request, in order that he might return to work. He felt well and was to report to the out-patient department for further treatment.

Case 5.—The patient was a white woman, aged 23, married, who had been treated for syphilis with neoarsphenamine. Jaundice had developed one week before admission. She was discharged feeling well but with a residual jaundice.

A pertinent question is whether sodium dehydrocholate has any vitiating effect on the pharmacologic action of the arsphenamine. The case which follows answers this by showing that a syphilitic lesion of the tongue progressed favourably under treatment with a combination of sodium dehydrocholate and neoarsphenamine. In this patient a gastro-intestinal type of reaction developed.

Case 6.—A white man, aged 23, married, had been treated for syphilis in the out-patient department. Before his admission to the hospital, the first injection of neoarsphenamine, 0.3 gm., caused no reaction; after the second injection of 0.45 gm. nausea and vomiting occurred, which lasted two days. He then went to a private physician for further treatment. After the next injection of neoarsphenamine, 0.45 gm., given by his doctor, vomiting, fever, slight jaundice, fainting spells and mild mental disturbance occurred.

Following this upset, he was referred to the house service by his physician. On admission, he was slightly jaundiced and somewhat disoriented as to time and place. There was a punched-out, active, syphilitic lesion on the tongue and ulcerated, membranous lesions of the throat.

The patient was given five injections of neoarsphenamine, the dosage being 0.3 gm. The first dose was mixed with 10 c.cm. of 20 per cent sodium dehydrocholate. He complained of a bitter taste and vomited immediately after the injection, but felt well thereafter. The subsequent four injections were mixed with 10 c.cm. of 5 per cent solution and were not accompanied by any disturbance. The tongue and throat cleared up almost entirely, and he was discharged eighteen days later to his private physician, who gave him three injections of neoarsphenamine, the dosage being 0.3 gm., and each dose being mixed with 10 c.cm. of a 5 per cent solution of sodium dehydrocholate. There were no subsequent reactions. The doses of neoarsphenamine were all made up with distilled water in a strength of 0.15 gm. to each 5 c.cm. of water.

Not all patients with the same type of reaction as that of the patient whose case has just been reported have done so well. Of eight others, one apparently received no benefit from the treatment, and one had doubtful benefit.

SUMMARY

Sodium dehydrocholate is a choleric drug, non-toxic in doses of 10 c.cm. of a 5 per cent solution administered intravenously at intervals of several days.

It has been used to combat the toxic action of arsphenamine and its derivatives on the liver.

In five cases of jaundice which developed during antisyphilitic treatment with arsphenamine the patients were treated with sodium dehydrocholate. There was a prompt fall of the icteric index, with rapid recovery. No explanation is given at this time, but it is suggested that the effect may be

caused by the washing of arsenic from the liver, owing to increased choleræsis.

In a number of cases in which nausea and vomiting followed intravenous injections of neoarsphenamine, the patients were treated by mixing the solution of the drug with a solution of sodium dehydrocholate and injecting the mixture intravenously. The majority of the patients showed no reactions following these injections. One case is reported in detail.

CONCLUSION

By the use of sodium dehydrocholate administered intravenously, two types of reaction to neoarsphenamine can be combated, jaundice and the gastro-intestinal reactions of nausea and vomiting. This is of utmost value for patients requiring vigorous treatment for an active syphilitic infection, as the reactions would ordinarily prohibit the use of arsenicals.

The Diagnosis and Treatment of Subacute Combined Degeneration of the Spinal Cord

By T. KAY MACLACHLAN, M.A.

M.B. (Camb.), F.R.F.P.S.

(From the Medical Press and Circular Supplement, 26th July, 1933, p. xv)

INTEREST has been renewed in this condition during the last six years following the great advance in treatment of Addison's (pernicious) anaemia by liver and its extracts, as initiated by Minot and Murphy; more especially as the prognosis of this nervous disease, so often associated with pernicious anaemia, had formerly been extremely bad.

Subacute combined degeneration of the cord is a condition named from its histological picture. Degenerative changes are seen in the posterior and lateral columns of the cord, and in advanced cases practically all the white matter of the cord may show absence of myelin, while the brain also may show some shrinking due to demyelination, especially in the fronto-parietal regions. The disease tends to commence in the mid-dorsal segments of the cord where the blood supply is poorest; it is thought to be of a degenerative rather than of an inflammatory or a vascular nature, and the striking feature is the absence of the neuroglial overgrowth which takes place in other conditions of the cord whether they be of inflammatory or degenerative origin. The condition is frequently associated with Addison's anaemia, but may also occur with severe anaemia due to other causes, with lymphatic leucæmia, and with cachetic conditions.

Although subacute combined degeneration of the spinal cord is established as a definite clinical entity, yet combined disease of the afferent and efferent system of the cord may occur in association with several conditions, namely, disseminate sclerosis, Friedrich's ataxy, meningomyelitis, myelitis, lathyrism and pellagra, as well as in some syphilitic conditions where changes in the cord produced by interference with the vascular or lymphatic circulation may cause a similar picture.

One should not now be satisfied with a diagnosis of 'spastic paraplegia', or 'ataxic paraplegia', although these were included till recently, in some textbooks, as diseases of the nervous system.

Subacute combined degeneration of the cord was formerly thought to be a late association of pernicious anaemia, and while it is true that symptoms referable to the nervous system, especially numbness and tingling in the extremities can be found in the majority of patients suffering from pernicious anaemia, it must be remembered that similar symptoms may occur in any severe anaemia or cachetic state, and that one is not justified in diagnosing subacute combined degeneration on the presence of any nervous symptoms, even though there is no doubt clinically about the diagnosis of pernicious anaemia.

The criteria on which subacute combined degeneration has been diagnosed probably to some extent accounts for the extreme variations described by different observers in the response to treatment. It must, however, be remembered that subacute combined degeneration may be quite definitely present before there is any evidence clinically, or even hematologically, of pernicious anaemia, as ignorance of this point appears to be the reason why certain cases are so very far advanced before a diagnosis is made.

The diagnosis is not always straightforward, as the clinical picture varies, dependent on the relative affection of the posterior columns, pyramidal tracts, or peripheral nerves.

The earliest symptoms are usually paresthesiæ, numbness and tingling in the lower limbs, and later the patient is aware of some clumsiness and weakness, and becomes less steady on the feet. Sensory examination shows some loss of vibration and joint sense, with perhaps some diminution in sensation to pressure and light touch. Less commonly there are pain, formication or a feeling of icy coldness, but lightning pains resembling those of tabes have been described. Later a girdle sensation, which may even be painful, develops and paresthesiæ also affect the hands.

It is usual thereafter to get involvement of the motor system, with a history of the limbs becoming easily tired, and later of one or both being dragged and feeling stiff, and this, with exaggerated deep reflexes, a positive Romberg's sign, clonus and extensor plantar responses, led to the condition being formerly known from its clinical features as ataxic paraplegia.

When the paraplegia becomes marked, dysuria is usually noted, while if untreated the paraplegia becomes complete, and the trunk and arms are also involved, although usually the shoulder and upper arm muscles are little affected. In the later stages wasting of the muscles with loss of electrical response occurs, and a flaccid paralysis with absent knee-jerks, but an extensor plantar response, is seen, and there is incontinence of rectum and bladder. Less frequently the picture is one of flaccid ataxy with early loss of reflex activity, and evidence of posterior column involvement, but even in these flaccid cases an extensor plantar response is usually obtained.

In the typical cases the sensory loss commences at the periphery, and tends to be of a glove and stocking distribution, while when it extends upwards to reach the trunk, its progress is usually limited by segmental lines. Trophic changes are common when the disease is well established, and bed sores are then difficult to prevent. Vasomotor disturbances at the periphery of limbs also occur, and oedema is occasionally seen.

In the advanced case, evidence of involvement of the cerebrum is not uncommon, being evidenced by confusion, drowsiness, and occasionally by delirium. Changes in the pupils and their reactions also occur, nystagmus may be present, and optic atrophy is occasionally observed, while if the disease has reached the lower cervical region involvement of the sympathetic fibres may be noted.

There may be no evidence of Addison's anaemia, but this is exceptional, it being usual to find at least megalocytosis with high colour index. The tongue often indicates an existing or previous glossitis, but even a history of a painful tongue or recurring digestive upsets are of value in helping to confirm one's diagnosis. For further confirmation, the fractional test-meal should never be omitted, especially if the blood examination is not helpful, as complete or relative achlorhydria is found in practically all cases.

DIAGNOSIS

If when first seen the patient presents the picture of an ataxic paraplegia with some loss of postural and vibratory sensation, various conditions have to be excluded. Tabes, as well as specific meningomyelitis, must be eliminated by a routine examination of the spinal fluid as well as of the blood.

In support of a diagnosis of disseminate sclerosis there would be a more rapid onset, and one would look for a history of diplopia, or of transient paresis, blindness, paræsthesia, or sphincter involvement; while nystagmus, absent abdominal reflexes, intention tremor or other lesions suggesting scattered involvement of the nervous system would be of confirmatory value. A paretic or luetic colloidal gold reaction in the spinal fluid in the absence of other evidence of syphilis would be of further diagnostic help.

If the girdle sensation or root pains were striking in addition to paraplegia and sphincter trouble, new growth of the spinal cord or its coverings would have to be excluded. Evidence of segmental sensory loss with perhaps a level of hyperalgesia, as well as pain and limitation of movement of the vertebra, should call for x-ray examination of the spine, and this, together with Queckenstedt's test and examination of the spinal fluid for xanthochromia and for dissociation between the amount of albumin and the cell count, should establish or exclude the possibility of tumour. Lipiodol radiography is occasionally helpful.

In elderly patients the occurrence of paresis and paræsthesia in the lower limbs as a result of vascular degenerative changes interfering with the nutrition of the spinal cord must be considered.

The age at onset, the family history, as well as nystagmus and skeletal deformities, help to distinguish Friedrich's ataxia from subacute combined degeneration, while residence abroad, a diet containing lathyrus sativus, and the simultaneous occurrence of several cases would suggest that lathyrism was the cause of the paraplegia.

Pellagra is uncommon in this country, but a history of a deficient dietary, and the characteristic lesions of the skin, as well as the affection of the nervous and alimentary systems and the tendency to exacerbations in the spring of the year, should establish the diagnosis. It must be remembered, however, that the disease may occasionally occur without the cutaneous lesions.

TREATMENT

There has been considerable difference of opinion as to whether liver, which is usually of such signal value in Addison's anemia, is of comparable value in subacute combined degeneration of the cord. Some writers have claimed that all signs and symptoms of cord disease may disappear, while others have found liver ineffective, not only in causing no material improvement, but even in staying the advance of the disease.

We have already noted that the picture of degeneration of the spinal cord may precede any outward clinical evidence of pernicious anemia, and in these days when the anemia can be so easily and quickly controlled by liver at its onset, the dose of liver necessary for the treatment of anemia *per se* need not be large for long. The failures in liver treatment of subacute combined degeneration of the spinal cord can often be traced to the employment of only those doses of liver which have been found sufficient to produce blood regeneration.

To treat the neurological condition it is essential that the liver must be pushed to a greater degree, and at the onset it should be given both in the form of one of the intramuscular injections as well as by mouth, and both fresh liver and the extract should be administered by the latter route. As in pernicious anemia, the response is better if the patient is able to take the fresh liver uncooked, and the daily dietetic routine can be made easier by the employment of the various recipes for the preparation of liver which have been published by Florence Irwin.

In combined degeneration of the cord one cannot be satisfied with a definite reticulocytosis, and an increasing red cell count as indication that improvement in the nervous condition is occurring. It must be our object to waste no time in arresting the changes in the spinal cord, and it has been found that a red

cell count of five millions is the standard at which one expects improvement in the cord symptoms, and not until this figure has been obtained should intensive liver therapy be discontinued. Nevertheless, one cannot expect regeneration in cases where nerve fibres have been destroyed, since nerve tissue cannot regenerate; but many of the symptoms have only been caused by the pressure of the swollen myelin sheaths and intensive liver therapy, even in cases only diagnosed when the condition is well-established, can usually relieve some of the symptoms. There are now many preparations of liver extract for oral administration on the market, and the equivalent of half a pound of liver as well as the same amount of the fresh gland should be given daily.

Following Gänsslen's production of extracts, potent by intramuscular or intravenous injection, the proprietary preparations Campolan and Hepatex are now available, and at the onset the equivalent of 500 grams of fresh liver should be given daily by injection.

Formerly in cases with marked anemia not diagnosed until an advanced stage, blood transfusion was often required, as the patient's anorexia and enfeebled general condition made adequate liver therapy by mouth impossible. Now even if the nature of the nervous disease is not recognized until the anemia is marked, transfusion is seldom necessary, or even intravenous injection, as an ampoule of campolan twice daily intramuscularly is usually sufficient to initiate a remission.

The rise in the cost of mammalian liver since its value in anemia has become generally known, and the greater expense of the liver extracts has made treatment a serious economic problem in the case of sufferers from subacute combined degeneration of the cord, where treatment must be pushed to a much greater extent than in pernicious anemia. In this connection the work of Davidson, in Aberdeen, in the preparation of a fish-liver extract promises to be of great value, as this extract has been found to be much more potent and more rapid in action than mammalian liver, while the cost to the patient should be much less.

Ventriculin, or other preparation of hog's stomach which has a similar effect to liver in promoting blood regeneration, may be used in place of a liver extract, but, as with the latter, it must be pushed to a greater extent than in treating anemia alone, and 30 to 40 grams daily should be given. The same remarks, however, do not apply to brain, which has been found to be of some value in inducing blood regeneration.

In treating pernicious anemia, Ungley found that the potency of brain in producing increase of the reticulocytes and red cells is only a third that of liver, but as regard the effects on the nervous system, brain has been found by him to produce definite neurological improvement in doses which would have relatively little effect compared with liver on blood regeneration. Brain is most potent given raw, and can be administered in the form of purée flavoured with tomato or orange juice. A dosage of about 480 grams daily should be employed.

More recently Sargent, maintaining that some cases of subacute combined degeneration were not improved by liver therapy, and that simple achlorhydric anemia might be the cause of the persistence of neurological symptoms in certain cases, discarded liver therapy in favour of massive doses of iron, and from this treatment excellent neurological results were reported, and even hematological improvement took place in some patients when liver had been found to be ineffective. In these cases (simple achlorhydric anemia) Bland's pill in doses of 150 grains daily may be used, and such an amount is usually well tolerated, even for the usual period of two or three months, before a reduction is made to a maintenance dose of 30-40 grains daily. It has been suggested that pernicious anemia and subacute combined degeneration of the spinal cord are deficiency diseases, and Mellanby has experimentally produced a condition similar to subacute combined

degeneration, even with mental affection, by diets deficient in vitamin A. He was able to relieve the neurological condition by incorporating vitamin A or carotene in the diet.

Strauss and Castle have shown that in pernicious anæmia there is absence of a normal 'intrinsic factor' in the gastric juice. Normally this factor acts on protein in the diet to produce a hæmatopoietic hormone, and the latter reacts with an essential 'extrinsic factor', believed to be vitamin B₁₂, to cause hæmatopoiesis. By further experimental work they conclude that vitamin B₁₂ is the extrinsic factor necessary for hæmatopoiesis, and that deficiency of vitamin B₁₂ is the cause of the neurological symptoms. These investigations have led to the employment of yeast, which contains vitamins B₁ and B₁₂, in the treatment of pernicious anæmia and subacute combined degeneration of the cord. For those unable to take ordinary yeast regularly this difficulty has been overcome by giving marmite, which is much more palatable, and a teaspoonful of this preparation should be given daily in sandwiches or added to gravy, while as a further variation bemax can be employed. If the diet does not contain adequate vitamin A, then the latter can be supplied by giving avoleum, radiostoleum or adexolin.

More recently Morris and his assistants have shown that a hæmatopoietic response can be produced in pernicious anæmia by the intramuscular injection of gastric juice. The antianæmic substance, 'addisin', which is probably a hormone, is destroyed by heat, and the juice has to be concentrated by distillation *in vacuo*. Amounts of this concentrate equivalent to 300-500 c.c. of gastric juice, while shown to be potent in the treatment of the anæmia, have yet to have their value proved in subacute combined degeneration of the cord.

Apart from what may be considered the specific treatment of the disease, there are other therapeutic measures directed to conditions frequently associated, which if ignored lessen considerably the efficacy of the methods we have already mentioned. Fever is not uncommonly present during the course of Addison's anæmia, and it does not appear to inhibit the action of liver, but if it is actually caused by any inflammatory or septic process such as cholecystitis, cystitis, or bedsores, then one finds definite inhibition of the normal response of neurological symptoms to treatment.

As in all nervous diseases, it must first be ascertained whether the bladder is functioning normally, or whether there is a bacilluria or pyuria. Direct questions must be asked in this connection regarding any dysuria, and it is well, even if the patient appears to be passing urine freely, to pass a catheter and find if there is any residual urine, as retention and decomposition of such often initiates a cystitis. Urinary antiseptics or lavage may be necessary.

Bedsores are of much worse import, especially if associated with incontinence of urine and feces, and if diagnosis and treatment have been delayed they often precipitate a fatal issue. Any focal sepsis, whether in skin, teeth, nasal sinuses, or elsewhere must receive treatment, and constipation must, of course, be controlled.

Some patients with subacute combined degeneration manifest evidence of hypothyroidism with malar flush, dry scaly skin, deficient perspiration, increased sensitivity to cold, and lowered B.M.R., and much general improvement may follow the administration of adequate doses of thyroid. The gastric deficiencies should also be made good, and the following mixture should be taken in a tumbler of water with the three main meals of the day:

R. Acid hydrochlor. dil.	dram 1-2
Glycerin pepsin	dram 1
Syr. lemonis.	dram ½
Aq. ad.	oz. ½

If there is indication of intestinal decomposition, the administration of charcoal or diinol after meals may be helpful, while abdominal massage, recumbency after meals, or a supporting belt should be advised if there is evidence of visceroptosis. Massage and passive movements are of value in spastic cases, or in those debilitated by long residence in bed, and re-educative exercises are of the greatest help to those patients who have improved to the extent of commencing to walk again, as well as for those whose hands had become clumsy for fine movements.

The outlook of patients suffering from subacute combined degeneration of the spinal cord, formerly so hopeless, has been greatly improved within the last few years, but diagnosis still tends to be made too late to obtain the full advantage of the therapeutic measures now available.

Reviews

CORRECTION

FUNGUS DISEASES: A CLINICO-MYCOLOGICAL TEXT.—By H. P. Jacobson, M.D. London: Baillière, Tindall and Cox, 1932. Pp. 317, with 153 illustrations. Price, 31s. 6d.

We regret that in our issue of June last, p. 353, when our review of the above book was published the price was stated to be 3s. and it should have been 31s. 6d.

Editor, I. M. G.

PHYSICAL CHEMISTRY OF LIVING TISSUES AND LIFE PROCESSES.—By R. Bentner, M.D., Ph.D. London: Baillière, Tindall and Cox, 1933. Pp. x plus 338, with 79 figures. Price, 29s.

The author has considered life as a scientific problem and, in attempting to study the problem in its various aspects, he has had recourse to the methods of colloid and electrochemistry—two of the main branches of physical chemistry. By preparing different artificial imitations of various single phases of life, he has tried to elucidate some of the most important problems of physiology, mainly connected with electrical currents in tissues and their relation to life processes. The book is made still more attractive because in its concluding

chapters it indicates in a clear manner the lines of future research in this direction, with the probability of enormous fruitfulness. If one requires further proof of the already established fact that methods of physical chemistry are essential for future researches in physiology, one is advised to read this book. It is needless to mention that the book will be of immense help to both physiologists and physical chemists.

R. N. C.

CAUSAL FACTORS IN TUBERCULOSIS.—By F. C. S. Bradbury, M.D., D.P.H. Published by The National Association for the Prevention of Tuberculosis, Tavistock Square, London, 1933. Price, 2s., post free.

The book contains 126 pages and embodies the report of an enquiry into the increased incidence of tuberculosis in certain Tyne-side districts in England. The National Tuberculosis Association financed the enquiry and Dr. Bradbury, a tuberculosis officer of the Lancashire County Council, conducted it. The investigation shows the stamp of thoroughness and care necessary for an intensive study of tuberculosis in a limited area, and brings forward, with the help of modern statistical

methods, the relative importance of economic, sociological and medical factors which may predispose to a high incidence of tuberculosis.

The two towns selected were Jarrow, which had a tuberculosis death rate of 2 per 1,000, and Blaydon where the rate was half of this. A house-to-house visit was made for collecting the necessary data on such factors as over-crowding, under-nourishment, insanitation, occupation of tenements, race, effect of early marriage, size and composition of family, poverty and house-to-tenant infection, always keeping as controls some non-tuberculous families. The clinical forms of tuberculosis prevalent in the area are analysed in part II of the monograph.

It has been shown that poverty has a marked statistical association with tuberculosis and that the chief methods by which poverty is found to cause tuberculosis are over-crowding and under-nourishment. The association of tuberculosis with poverty is greater than with most of the other factors studied. Over-crowding occupies a high position in the list of factors which contribute to the prevalence of tuberculosis in the areas dealt with. The standard of over-crowding has been taken as two or more persons living in one room. If the average income per head per week is less than ten shillings, families have been classed as poor. If the allowance per head per week has been less than one pound each of meat and butter and one pint of milk per head per day, the families have been labelled as under-nourished. Families of five or more persons have been classed as large families. A woman who married before the age of twenty-one has been regarded as having married early and is referred to as a young mother.

By following these standards it has been found that under-nourishment, particularly with regard to meat, bread, butter and fresh milk, is an important predisposing cause of tuberculosis and, in fact, of sickness in general. It has been further suggested that of the food-stuffs mentioned, fresh milk is of greater importance than the others as a preventive of tuberculosis in an urban population.

Over-crowding occupies a high position in the list of factors associated with tuberculosis, but it is not well understood as to why this is so.

Analyses of racial peculiarities have shown a considerable Irish element which forms about fourteen per cent of the population in Jarrow and only three and a half per cent in Blaydon, and it has been shown that there is more tuberculosis in Irish than in English families. After eliminating such correction factors as the relative size of families, it was found that earlier age and sex constitution are of little importance when compared with English families in which the mortality is much lower. Hence the conclusion has been drawn that the cause of the higher incidence of tuberculosis in the Irish is a relative want of immunity or racial susceptibility to the disease.

Conditions such as insanitation, bad ventilation, dirt, damp, house-to-tenant infection and the local peculiarity of women marrying at an unusually early age have been studied as being possible contributory factors but, though they may be of some importance as predisposing causes of tuberculosis, it is considered that their association with tuberculosis can be adequately explained on other grounds.

The investigation has brought to light the important fact that the supervision exercised by maternity and child-welfare clinics is a definite factor of importance in the suppression of tuberculosis. It has been noted that tuberculosis is more prevalent in families with children than in families without children, and is more prevalent in large than in small families.

Part II of the report deals with the findings from the clinical details regarding 1,033 patients who were on the registers of the Jarrow and Blaydon tuberculosis dispensaries between 1926 to 1930. It has been noted that the excessive mortality from pulmonary tuberculosis in Jarrow is especially marked in the 0 to 15 and 15 to 25 age groups, particularly in the former. In

females the maximum mortality occurs in the 15 to 25 age group, as in England and Wales. But the maximum in males in this area (Jarrow) occurs also in the 15 to 25 age group, thus differing markedly from England and Wales, where the maximum occurs in the 45 to 65 age group. It has been further found that the population of Jarrow suffers from a more rapidly fatal type of the disease. It has been suggested that the principal factors causing this are the relatively greater susceptibility of the population and the unfavourable home conditions. The high death rate from pulmonary tuberculosis in the 0 to 15 age group has been thought to be due to the unfavourable environmental condition prevalent in the area.

Non-pulmonary tuberculosis has been found to show certain peculiarities in Jarrow, particularly the unusually high incidence of abdominal tuberculosis. From the very limited use of fresh milk in the area it is thought that the high incidence of pulmonary tuberculosis is the chief contributory factor to the high incidence of non-pulmonary tuberculosis, largely owing to the increased opportunities for infection which occur through over-crowding and other adverse factors which are so prevalent in Jarrow.

The following conclusions arrived at by the committee will be found of practical value in reducing the incidence of tuberculosis:—

(1) The building and use of tenement dwellings should be strictly controlled, particularly in regard to the size and number of rooms, the number of persons who occupy them and the general sanitary condition of the dwellings.

(2) In view of the apparent importance of under-nourishment as a predisposing cause of tuberculosis, it is desirable that attempts be made to improve the defences of poor families against tuberculosis by providing adequate and balanced diets at the cheapest possible rates.

(3) Fresh milk, free from tubercle bacilli, especially in poor families, children, should be regarded as a daily dietary.

(4) The facilities provided by maternity and child-welfare clinics should be more widely used. The aim should be to have the fullest possible liaison between the Maternity and Child Welfare and Tuberculosis Departments.

The numerous conditions, which have been shown in the report to be associated with tuberculosis, suggest that collective action can deal with the disease at the source, whereas the ability of the individual to protect himself against it is more limited. The association's policy of active propaganda, to educate the public in matters concerning tuberculosis, has been thought a very necessary and valuable means of combating the disease.

We draw the attention of all workers who are interested in the question of the causation and prevention of tuberculosis, to this report which we consider to be a valuable contribution to our knowledge of some factors underlying differences in the incidence and character of tuberculosis in various areas. We join with the committee members in hoping that this report may stimulate the organization of similar intensive investigations in other areas. The work already done in rural and urban areas by us in India strikingly agrees with several of the findings of the committee.

A. C. U.

'STUDIES IN THE PHYSIOLOGY OF THE EYE'.
Still Reactions: Sleep: Dreams: Hibernation: Repression: Hypnosis: Narcosis: Coma and its Allied Conditions.—By J. Grandson Byrne. London: H. K. Lewis and Co., Ltd., 1933. Pp. xii plus 416, with 47 illustrations. Price, 40s.

A BETTER title for this most interesting book would have been 'Studies in the Physiology of Vision', using the word Vision in its widest sense. The book will appeal not only to physiologists and ophthalmologists but also to psychologists. In this last group are included

all those practitioners who are interested in the mental health of their patients. In fact it is mainly for this last group that the book has been written and the following extract from the last paragraph of the final chapter illustrates this.

The author is referring to the results of his experiments spread over a period of twenty years and he says:—

'They also, in my opinion, furnish the means for a better understanding of the physiological processes that underlie, or are associated with all mental activity, and consequently may furnish in addition the solid foundation for a therapy-preventive and restorative based upon psychoanalysis—which shall not be too mystifying or metaphysical, but scientific and practical, and above all available for extensive use by the medical practitioner.'

And that in the reviewer's opinion is just exactly what is wanted in these days. Each chapter is followed by a summary of the results of the experiments which is both lucid and convincing and each summary is followed by an exhaustive bibliography.

H. S. C.

DIABETES IN CHILDHOOD AND ADOLESCENCE.—

By Priscilla White, M.D. Published by Henry Kimpton, London. Pp. 236, illustrated with 25 engravings and a coloured plate. Price, 18s. net.

THE diabetic child should prove to be of more than usual interest to those working on the subject, not only because it provides them with pure diabetic lesions unaccompanied and uncomplicated by degenerative changes due to age, but also because it gives them a wider field in following up individual cases in the different periods of their lives. Herein lies the great value of Dr. Priscilla White's book, for not only has she made elaborate and exhaustive clinical studies based on over 700 cases, but also she has literally lived with her young diabetic patients, which gave her the unique opportunity of a very close and intimate study of individual cases, a thing not possible otherwise.

Dr. White's book deals with the whole subject exhaustively in all its aspects, physiological, pathological and practical, and should prove to be of great value to everyone working on the subject.

J. P. B.

VITAMINS AND OTHER DIETARY ESSENTIALS.—

By W. R. Aykroyd, M.D. London: William Heinemann (Medical Books), Ltd., 1933. Pp. 218. Price, 7s. 6d.

THIS book published at the price of the usual novel might well replace the next purchase of regular novel readers, for within its pages they will find entertainment combined with a great deal of sound information which is set out in such a way that it can be easily applied to the selection of food in any middle class home.

The first few chapters deal with general dietetic factors and are followed by seven chapters in which the various diseases due to vitamin deficiency are discussed, and several final chapters deal with diet on a broader basis. The book is clearly and simply written and the author has the power of trenchant criticism and epigrammatic phraseology which makes the reading of it a real pleasure. It can be taken up by any one who is wholly ignorant of the subject of dietetics and there is nothing in it such a person cannot understand. It is accordingly an excellent book for a beginner and it is a pity the author did not give a list of references of the authorities to which he refers and thereby enable the beginner to delve further into the subject. One of the most valuable characteristics of the book is that it has put vitamins back in their proper place in the dietary scheme, for when Professor Hopkins first used the term he defined vitamins as accessory food factors and many subsequent writers apparently forgot the word accessory and seemed to look on vitamins as the food itself. The author also tells where a supply of vitamins may be had in ordinary articles of diet instead of giving

the impression they are only obtainable in expensive special preparations.

It is a book which will be of value to medical men as well as to the lay public, by whom it may be read with complete understanding.

P. A. M.

THE SANITARY INSPECTOR'S HANDBOOK.—By

H. H. Clay, F.R.San.I., F.I.S.E. London: H. K. Lowis and Co., Ltd., 1933. Pp. xx plus 386, with 93 illustrations. Price, 15s.

WITHIN the compass of less than four hundred pages the author has written on all subjects with which a Sanitary Inspector has to deal in the discharge of his duties in various capacities in a country where the sanitary laws have made tremendous progress in all directions bearing on health. The book starts with the evolution of public health law; the outstanding events given in the chapter are well calculated to inculcate into a would-be sanitary inspector enthusiasm for the study while the full list of duties and the details of the training will form an admirable introduction to it. All the chapters which follow bear the stamp of the experience and acumen of the author; they are remarkably up-to-date, as a rule complete, and yet concise; the instructions cover all aspects of the subject, are eminently practical, and have been fittingly based on various sections of the corresponding Acts, Regulations and Orders. The following comments, however, may not be out of place:—

On page 121, line 3, while advising a reservoir of non-metallic material for storage of rain water, the attention of the reader might be drawn to the highly aerated and very soft character of the water and the consequent risk of a metal, like lead, being dissolved by it. In chlorinating water which is also filtered, as advised in the last two lines on page 136, will the quantity of chloride of lime added be the same as in the treatment of polluted water, viz, one part of free chlorine available per million of water? Under the heading of water softening, pp. 137–139, the base-exchange method has been described simply as an alternative to the softening by heating or by adding lime, but the special merit of the former lies in its ability to free the water both from temporary as well as permanent hardness while the latter can remove the temporary hardness only. On page 139, we read 'These possess the power of absorbing lime and magnesia salts, and replacing them with their equivalent of bicarbonates as, for example, bicarbonates of soda'; this line is misleading. It would be clearer to say that the process replaces calcium and magnesium salts with the equivalent of corresponding sodium salts, viz, carbonates of soda in the case of carbonates of calcium and magnesium, and sulphate of soda in the case of sulphate of calcium and magnesium.

Sampling water for bacteriological analysis is delicate work; not only should the sample bottle be a thoroughly sterilized one which after filling should be packed in ice, as advised on page 140, but every precaution should be taken against contaminating the water in any way during sampling it, for which there might be specific directions for the students. While the bottle for the sample for chemical analysis should be washed thoroughly with the same water before filling, as advised in the previous page, this will not only be unnecessary but undesirable with the sterilized bacteriological bottle. Line 30 on page 271 reads 'milk should be presumed not genuine if it contains not less than three per cent of milk fat' the second 'not' was evidently inserted in error.

The book will be greatly appreciated by students preparing for the sanitary inspectorship examination; it will undoubtedly be also very useful to sanitary inspectors serving in Great Britain. In India, the people mostly live in villages under widely different conditions; but in towns the problems of public health are similar to though not exactly the same as those in England, and our sanitary laws and by-laws are based as a rule on English laws and regulations, so the sanitary officers

working in cities and towns of this country will find in the book, a valuable guide in carrying out the details of their duties and in advising their local authorities regarding improvement of sanitation and public health of their towns.

B. B. B.

FOOD AND THE PRINCIPLES OF DIETETICS.—By R. Hutchison, M.D., F.R.C.P., and V. H. Mottram, M.A. Seventh Edition. London: Edward Arnold and Co., 1933. Pp. xvi plus 630. Illustrated. Price, 21s.

Dr. Hutchison's name as a keen physician and a gifted clinical teacher is too well known in medical circles to need any special introduction. His book on 'Food and the Principles of Dietetics' was first published in the year 1900, and for the last 32 years it has successfully maintained its position as a standard work of reference on the subject. Our ideas on dietetics have undergone very extensive changes during recent years particularly on account of the recognition and isolation of the vitamins. In order to keep pace with this increase of knowledge the author has collaborated with Professor Mottram, and their joint efforts are represented in the seventh edition. This edition has been extensively revised and reset. The first three chapters have been completely re-written through the help of Professor Mottram. The coloured plates showing the food values of the common articles of food are novel features and are especially instructive. The new edition, we are confident, will not only maintain its well-earned popularity, but will enhance the prestige of its predecessors.

R. N. C.

ANATOMY OF THE EYE AND ORBIT. INCLUDING THE CENTRAL CONNECTIONS, DEVELOPMENT, AND COMPARATIVE ANATOMY OF THE VISUAL APPARATUS.—By E. Wolff, M.B., B.S. (Lond.), F.R.C.S. (Eng.). London: H. K. Lewis and Co., Ltd., 1933. Pp. viii plus 310, with 173 illustrations. Price, 31s. 6d.

This book will naturally appeal only to the specialist whose interest in anatomy does not extend beyond the orbit and its contents. It is beautifully illustrated, most of the figures being original, and the book is printed on heavy art paper. It is altogether a pleasing production and is a credit to both author and publishers, and the reviewer's only regret is that he cannot recommend it to the general medical public. The reasons of this are, that although the price is high when one considers the limited scope of the book it is not too much if the form of presentation of the subject is the criterion of its value; but when the reader can acquire nearly all the information given in the volume together with the anatomy of all the rest of the body for the expenditure of only a little more money, this book must be classed as a luxury and not a necessity to the profession at large.

MODERN PHARMACOLOGY AND THERAPEUTIC GUIDE.—By Akhil Ranjan Majumder, M.B. Published by S. P. Majumder, Calcutta. Third Edition. Pp. viii plus 602. Price, Rs. 5. (Obtainable from the Book Company, Ltd., Calcutta.)

This book was first published in 1929 to provide a handy manual to the students going up for the licentiate standard of the State Medical Faculty examinations. That the book has served its purpose and is a certain answer to the expressed need of the students is more than evident from the rapidity with which two editions were consumed and a third edition called for. The science of therapeutics and pharmacology is fast progressing and a good many additions have naturally been made to keep the book up to date. Amongst the important additions may be mentioned the chapters on immune therapy, on preparations of invalid foods, on the calorific and vitamin values of various food-stuffs in common use in India, and on radiotherapy. In writing the last-named chapter, the author has obtained

the services of a radiologist and technician. The numerous prescriptions appended in the footnote are features which cannot be passed by without comment. The beginner will appreciate it thoroughly in view of the fact that difficulties are usually met with in writing out a good recipe.

The book, we have little doubt, will be of assistance to those who have to revise rapidly their knowledge of pharmacology and therapeutics in general. To the worried student whose final examinations are within sight, the book will be a sympathetic friend. It should not, however, be forgotten that it is a sort of a synopsis of the vast subject of pharmacology and therapeutics, and cannot replace a standard and authoritative textbook; any attempt to make it serve this purpose will inevitably lead to failure.

MELIODOSIS.—By A. T. Stanton, C.M.G., M.D., F.R.C.P., and William Fletcher, M.D., M.R.C.P. London: John Bale, Sons and Danielsson, Ltd., 1932. Pp. lv plus 59, with 37 plates.

This is No. 21 of the studies from the Institute for Medical Research, Federated Malay States, and deals with the very deadly and fortunately rare disease Melioidosis. It was first reported in the *Indian Medical Gazette* in 1912 by Whitmore and Krishnaswami and since then of the 83 recorded cases only two have recovered and a correct diagnosis has been made before death in only nine cases. That the clinical diagnosis of melioidosis is difficult is well illustrated by the different diagnoses such as cholera, typhoid fever, malaria, amoebic abscess of the lungs, and glands that have been made in Ceylon, The Malay States, Ceylon and the Dutch East Indies are the only countries where melioidosis is known to attack animals and although cases of human infection have been so far reported from Burma and the Malay States only, we agree with the authors when they state that it is highly improbable that melioidosis is limited to the few places where its presence has been detected. Its symptoms are so varied and obscure that it is seldom diagnosed until after death, and then only in those places where a bacteriological examination can be made. Even when laboratory facilities are available the disease may escape recognition by those who are unfamiliar with it, because the bacillus grows so profusely that it is apt to be mistaken for a contamination.

The authors have dealt exhaustively with the clinical, pathological and bacteriological aspects of the disease in which they have been interested for a number of years. The illustrations which make up more than half the volume are a remarkable feature of this well prepared book.

This account of melioidosis should be in the hands of everyone who practises in the tropics and it is very probable that it will lead to the recognition of melioidosis in many parts of the world. This book will prove invaluable in laboratories engaged in the investigation of tropical diseases.

C. L. P.

DISEASES OF THE EYE.—By Ernst Fuchs. The 15th German Edition as revised by Professor M. Salzmann. Translated into English by E. V. L. Brown, Professor of Ophthalmology, University of Chicago. This is the 10th Edition in English. It has 255 illustrations and 41 coloured plates. Philadelphia and London: J. B. Lippincott Company, 1933. Pp. xviii plus 641, with 255 illustrations in the text and 41 coloured figures. Available from Messrs. Butterworth and Co. (India), Ltd., Calcutta. Price, Rs. 31-8.

'Fuchs' Ophthalmology' has been a household word to ophthalmologists for over 44 years. Each succeeding edition got larger and larger, as is usual, till the last edition became altogether too unwieldy. The present volume has been reduced by some 350 pages by the omission of the Introduction and the chapters on Examination of the Eye, Refraction, and Operations,

as well as the special chapter on Refraction by Douane. These omissions in no way detract from the value of the book and these subjects are fully dealt with in other publications.

This new edition of Fuchs is still essentially like the old one and will still be read, consulted, and quoted as one of the best and most comprehensive textbooks in ophthalmology. The value of this edition has been greatly increased by the addition of forty-one coloured drawings of fundus conditions, both normal and abnormal. These drawings have been made by a man who is, at the same time, an artist and an ophthalmologist of international repute, to wit, Professor Salzmann and who is also responsible for the revision of the 15th German Edition from which this translation has been made. Unfortunately that edition was published as long ago as 1924, so that this translation is out of date as regards, for example, recent surgical treatment of detached retina, the newer filtration operations for glaucoma, and so on.

The translation itself leaves a very great deal to be desired.

The German construction has been too closely followed and one is conscious throughout the book of a phraseology which is quite un-English. Often the translation of a word is not only inaccurate but even misleading. For instance to quote only a few examples:—a rifle bullet is translated as an 'infantry charge'; squeezing of the lids becomes 'knifing of the lids'; 'tearing' is used for laceration. This has the merit of being a much shorter word but it has no other merit. Then again 'vessel free' and 'vessel rich' are used for vascular and avascular.

Perhaps however these are only Americanisms. At any rate the English spelling is Americanized throughout the book and this does not add to its attractiveness.

All these defects are only minor ones and the book remains one of the best and most comprehensive textbooks on ophthalmology.

I notice that the beautiful coloured plates at the end of the book are produced in Germany. I assume that is why it is possible to retail the book at the comparatively low price of Rs. 31-8.

H. S. C.

THE TREATMENT OF FUNCTIONAL NERVE CASES BY THE METHOD OF NEURO-INDUCTION.—

By Leonard Inkster, M.A. (Oxon.), M.R.C.S., etc. London: H. K. Lewis and Co., Ltd., 1933. Pp. vii plus 78. Price, 3s. 6d. net.

ALL books on psychotherapy are characterized by a dominant note of optimism with regard to the treatment of the various maladies which the 'flesh is heir to'. This book is no exception. Written in an easy-flowing and attractive style, the book enthusiastically stands for a method of neuro-induction which was originally enunciated by Dr. Heydn Brown. Neuro-induction is a form of treatment in which we aim at securing and keeping a state of absolute relaxation of mind and body. It is neither psychoanalysis nor hypnosis nor 'conscious suggestion' in the sense in which these terms are commonly used. It is a sure and even an easy method to practise. The technique is best explained in the words of the author:—'When, at the request of another, the patient lets the hand down and lowers the eyelids, relaxation occurs.'

By following this technique of neuro-induction the author reports very encouraging results in a large variety of cases. According to him, it brings ease of mind and body from the very beginning, and allows of a cumulatively increasing ease as the treatment continues. As an instance of the success of the method the author refers to cases of asthma where neuro-induction acts like adrenaline in relieving spasms and restoring normal tone to the arterioles.

The reviewer has not much experience in India of the method advocated and does not feel competent to give any opinion on the degree of success or failure of the method in the hands of expert psychotherapists.

It is however conceivable that a large measure of success will be obtained in cases where the mental factor is predominant.

R. N. C.

PHYSICAL CHEMISTRY FOR STUDENTS OF BIOLOGY AND MEDICINE.—By D. I. Hitchcock, Ph.D. London: Baillière, Tindall and Cox, 1932. Pp. xii plus 182, with 26 figures. Price, 15s. 6d.

A KNOWLEDGE of the rudiments of physical chemistry is essential to the proper understanding of the physiology of the human body; the subject is consequently an important part of any medical course. Physical chemistry is not usually a separate subject in the medical curriculum but the student is taught the necessary fundamentals of the subject in his chemistry and physiology courses. The writer of the book under review has collected into one volume twelve chapters on different physio-chemical subjects which are important to the medical student and essential to most medical research workers.

The subjects are dealt with concisely and in most cases clearly, but the author assumes a familiarity with chemical formulae and simple chemical reactions; this is justifiable but it does not make the book easy for the casual medical reader who has left chemistry behind him for some years. A useful feature of the book is the list of references; in each chapter not only is the reader referred to those authorities where he can read up the subject more fully but the special chapter of the books referred to is also indicated. It should prove a useful book to the medical student, and to the medical research worker who wishes to brush up this particular subject.

PITUITARY BODY AND HYPOTHALAMUS AND PARASYMPATHETIC NERVOUS SYSTEM.—By Harvey Cushing. London: Baillière, Tindall and Cox. Pp. viii plus 234, with 97 figures and 2 coloured plates. Price, 29s.

PROFESSOR HARVEY CUSHING is one of those international figures who have contributed materially to our knowledge of the pituitary body. In this book, an attempt has been made to collect some of his important lectures relating to the pituitary body, hypothalamus and the parasympathetic nervous system. The reader will find in these lectures a veritable mine of information regarding the physiology and pathology of the pituitary region of the brain, and the specialist will find a detailed and expert discussion of all those practical and theoretical problems of diagnosis and treatment which render tumours of the pituitary gland a difficult medical speciality. The richness of material available, the freedom with which the subject is presented and the elaborate discussions and analyses with which the central questions at issue are pursued, are features which mark the book as being above the average. Photographs and coloured plates which are well chosen and very suggestive are to be found in profusion. The get-up is excellent and leaves nothing to be desired. All those who are interested in pituitary surgery are advised to obtain a copy of the book.

R. N. C.

A TREATISE ON MATERIA MEDICA AND THERAPEUTICS.—By The late Rakhaldas Ghosh. (Thirteenth Edition by B. N. Ghosh, F.R.F.P. & S.) Calcutta: Hilton and Co. Pp. xv plus 712. Price, Rs. 7-8.

'MATERIA MEDICA and Therapeutics' by Dr. R. Ghosh first saw the light of day in the year 1901 and during the 32 years that have elapsed since then it has passed through thirteen editions. The twelfth edition had to be reprinted to meet the demands of medical students. This fact alone is a measure of the immense popularity of the book and shows in no unmistakable terms the useful purpose it is serving amongst the student

community. For many years, junior students in Indian medical schools and colleges have looked upon it as the standard book on the subject.

The system of teaching therapeutics followed in the early years of the twentieth century has undergone radical changes. Physiology and pharmacology are now considered to be the basis of treatment and pharmacology is now included in the medical curriculum to provide a scientific basis for the study of therapeutics. Any recent book on therapeutics which does not provide a groundwork of the broad pharmacological principles will therefore fail in its chief purpose. It is a pleasure to note that the author has not ignored the modern developments of pharmacology and has recast the book thoroughly in the light of modern teachings.

The publication of the new British Pharmacopœia, 1932, has necessitated many changes in that section of the book which deals with materia medica proper. Recent advances have also occurred in our knowledge regarding endocrines and vitamins and the author has not spared any pains in incorporating all the recent teachings in the present edition. A chapter on radiation therapy has been added and this will be of special value in view of the increasing attention that is manifest in the direction of treatment by means of radium and ultra-violet emanations. The chapter on Indian indigenous drugs is also worth special mention. It is high time that Indian students should learn the useful drugs that are available in their own country and can be used as cheap substitutes for the more expensive official preparations.

In a book of this nature typographical errors are very difficult to avoid and the reader will find a number of them. In the chapter on opium and morphine the author has remarked on the utility of narcotine in malaria. Though this was mentioned by the Royal Commission on Opium nearly thirty years ago, recent work has definitely disproved the statement.

Two of the most important discoveries in the realm of endocrinology are perhaps those concerning the manner in which the anterior pituitary gland controls reproduction and the action of vitamin A in maintaining resistance against infection. These matters have not received

proper attention. It is however hoped that these will be rectified in future editions.

R. N. C.

NATURAL CHILDBIRTH.—By G. Dick Read, M.D. (Cambridge). London: William Heinemann (Medical Books), Ltd., 1933. Pp. ix plus 127. Price, 7s. 6d.

DR. GRANTLY DICK READ has written a fascinating book, which will do much to achieve his ambition to 'initiate such change as will in future generations re-establish childbirth in the civilized races as a painless procedure'.

He does not accept the teaching that parturition must of necessity be a painful procedure; he does not believe that the modern woman is becoming more and more mechanically inefficient for a function on which the whole future of the race depends, and he has endeavoured in the book to fathom the problem of pain and its elimination during childbirth. It is a problem which every woman and all but the dullest men ponder over at some time, and Dr. Read's book opens up a very fruitful approach towards its solution.

His conclusion is that the instincts and accompanying emotions govern the type of labour. Fear in the modern civilized woman is often stronger than the emotions associated with the reproductive and parental instincts, and instead of the harmonious working of the reproductive organs and an easy birth under the strong stimulus of pleasing emotions, there is disquietude and even terror reflected in disharmonious working, impaired function, and a difficult birth.

Dr. Read has much sound advice to give to doctor and nurse alike on the preparation of the patient and the conduct of the confinement, and no practitioner who aspires to a reputation as a successful obstetrician and whose ambition is to leave each patient functionally perfect in her plural rôle of woman, wife and mother, can afford to neglect to read this book. It will give him a new viewpoint on childbirth, a deeper understanding of the woman in pregnancy and labour and will enable him to acquire that 'personality' which makes for success and which is too often thought to be the monopoly of those blessed by the gods.

Annual Reports

ALL-INDIA LEPROSY CONFERENCE

THIS conference convened by the British Empire Leprosy Relief Association was held at the All-India Institute of Hygiene and Public Health from the 27th to the 29th of March last. Twenty delegates attended, and a large amount of work was got through and several important papers dealing with the many aspects of the leprosy problem were read. Unfortunately lack of space prevents us giving abstracts of these papers, but we give below the resolutions and recommendations of the conference, which give a good idea of the extent of its activities.

RESOLUTIONS

Resolution I. Co-ordination and Organization.

In view of the wide prevalence, severity and infectiousness of leprosy in India it is resolved:

(a) That there is a great need for consolidation, co-ordination and extension of anti-leprosy work.

(b) That as leprosy is essentially a public health problem, every effort should be made to make anti-leprosy work an integral part of the public health system, using the latter term in its widest sense, i.e., in both its curative and preventive aspects.

(c) That it is desirable that in every province or state there should be a specially trained leprosy officer.

(d) That for the more efficient working of anti-leprosy measures a provincial or state leprosy board be formed in each province or state. This board should be chosen from representatives of the Medical and Health Departments, Mission to Lepers, British Empire Leprosy Relief Association and any other agency interested or engaged in leprosy work. The provincial leprosy officer should work in close collaboration with this board of which he may with advantage be a member. The functions of this board would be to co-ordinate all present and future anti-leprosy measures throughout the province.

(e) That similarly in each administrative district where leprosy is highly endemic there should be a special leprosy officer, who should work in close collaboration with the special leprosy officer of the province.

(f) That in such districts a district leprosy board should be constituted, consisting of the heads of the medical and health departments, and of any local leprosy organization, together with the senior government officials, representatives of the district board and of the public. The functions of this board will be to co-ordinate all anti-leprosy measures in the district. The local leprosy officer should work in close collaboration with this board.

Suggestion.

It is suggested—

(a) That the provincial or state leprosy board be convened by the Surgeon-General or the Inspector-General of Civil Hospitals in consultation with the Director of Public Health.

(b) That the district leprosy board be convened by the district magistrate in consultation with responsible district officers, medical and administrative.

Resolution II. Training

Because of great difficulties connected with anti-leprosy work (e.g., detection of early cases, treatment and prevention) it is resolved:

(a) That instruction in leprosy by a specially trained doctor should be included in the curriculum of all medical schools and colleges.

(b) That special courses should be given at convenient centres where clinical material is available to all government doctors. Private practitioners should be encouraged to attend these courses.

(c) That a more thorough training should be given in a suitable institution to district health officers and medical men engaged in special leprosy work. This course should be of at least a fortnight's duration.

(d) That all dispensers, employed by Government or local bodies, should be given a short course of training in leprosy; such a course should include practical instruction in the technique of injections.

(e) That sanitary inspectors should be trained so that they can recognize leprosy, and be able to aid in propaganda and survey work in the villages. This work should be done under the supervision of the district health officer in co-operation with the special leprosy officer where such exists.

(f) That other workers, such as sanitary or health visitors, public vaccinators, dais, etc., should be trained to recognize leprosy; local leprosy institutions might be used for this training.

(g) That all medical officers and others connected with the recruitment of industrial labour should be trained to recognize leprosy; and that all labourers should be examined for leprosy before recruitment and periodically afterwards.

Resolution III. Special Leprosy Clinics

The need for forming and maintaining an adequate standard of anti-leprosy work in rural areas is recognized. It is therefore resolved:

(a) That there should be in each administrative district where leprosy is highly endemic at least one model clinic under a whole-time leprosy officer. This clinic would act as a demonstration of the best methods of carrying out an anti-leprosy campaign; it would also act as a centre for prevention, and for the training of doctors and layworkers in the district and thus eventually lead to the establishment of other anti-leprosy centres.

(b) That a memorandum be prepared describing the functions and scope of the work of a model clinic and made available for distribution to all district officers, to medical, administrative and local bodies, and to those interested in the leprosy problem.

Resolution IV. Leprosy Clinics in General Hospitals

It is recognized that leprosy can be better treated in clinics especially devoted to that purpose, but in view of the large number of cases needing treatment, it is resolved that all government medical officers and local practitioners should be encouraged to treat leprosy and initiate anti-leprosy schemes along similar lines to those in the model clinics.

Resolution V. In-patient Institutions

Although emphasis is laid on the need for leprosy clinics to carry out treatment and prevention, the need for residential institutions has not diminished but rather increased. These institutions provide for the voluntary isolation of infectious patients and for the treatment

of cases the nature of which demands hospital care. It is therefore resolved:

(a) That the formation of voluntary isolation colonies be encouraged wherever possible.

(b) That the accommodation in the existing institutions be used to a greater extent for the isolation of infectious cases.

(c) That it is desirable that there should be, where possible, closer co-ordination between leprosy clinics and leprosy institutions.

Resolution VI. Research

It is recognized that highly specialized research is best done in efficiently equipped laboratories; but in order that other branches of research may be facilitated it is resolved:

(a) That more use should be made of the facilities in existing institutions and that the staffs of these institutions should be encouraged to undertake such work.

(b) That there is a need for the establishment of a special leprosy investigation centre in a suitable rural area in order to make an intensive study, over a prolonged period, into the epidemiology and control of leprosy.

Suggestion.

It is suggested that the British Empire Leprosy Relief Association might make arrangements for leprosy workers in the provinces to obtain any necessary literature bearing upon any particular aspect of the problem which they are studying.

Resolution VII. Leprosy in Children

Available statistics show that in endemic areas the incidence of leprosy in school children varies from 0.5 to 3 per cent. This conference is of the opinion that in such areas all school children should be examined for leprosy. Treatment should be provided for all definite cases found, and isolation of all infectious cases strongly urged.

RECOMMENDATIONS

(1) It is the opinion of the conference that in leprosy *general treatment* is of paramount importance. While there are many forms of *special treatment*, experience has shown that of the methods at present available the following are the most effective and practicable:—

Injections of hydnocarpus oil or esters with 4 per cent creosote, which may be given intramuscularly, subcutaneously or intradermally.

Since the intradermal method of injection requires more skill and time than the other two methods, its use should be chiefly confined to in-patients; it can however be used in out-patient clinics in suitable cases, provided sufficient time and skill are available; otherwise in out-patient clinics intramuscular and subcutaneous infiltration should be used.

(2) Whatever method of injection is used, the effects can be intensified by local application of trichloroacetic acid solution.

(3) An opinion has frequently been asked regarding the relative value of hydnocarpus oil and esters in the treatment of leprosy. While the esters have been declared by many workers to be the more effective of the two, the opinion of this conference is that the oil is almost if not quite as effective as the esters. It has the advantages of being cheaper and uniformly less irritant, while the disadvantage of its greater viscosity can be overcome by heating it sufficiently before injection. Any possible advantages of esters may be counter-balanced by the possibility of treating larger numbers of patients by the cheaper drug.

(4) While many patients can be treated effectively as out-patients, there are others who, because of complicating conditions, cannot improve without careful examination and treatment in hospital. It is therefore important that there should be beds where such patients may be kept temporarily under observation and treatment.

Captain H. W. Mulligan, Assistant Director, Malaria Survey of India, on foreign service under the Indian Research Fund Association, is granted leave for 1 month, with effect from the 1st September, 1933, or subsequent date from which he may avail himself of the leave. His services are replaced at the disposal of the Director-General, Indian Medical Service, with effect from the date on which he proceeds on leave.

PROMOTIONS

Colonel to be Major-General

H. R. Nutt, V.H.S. Dated 20th July, 1933.

The provisional promotion to the rank of Major of the undermentioned officers is confirmed:—

D. P. Bhargava.

B. R. Tandon.

Lieutenant to be Captain

W. Fleming. Dated 22nd May, 1933.

Note

LIVOGEN

DESCRIPTION

LIVOGEN is a highly concentrated liquid preparation containing in one fluid ounce the whole of the hæmatopoietic principles (including vitamin B) of four ounces of fresh liver. It contains additional vitamin B extract equivalent to one ounce of fresh yeast in each fluid ounce, together with five grains of hæmoglobin for the supply of iron in readily-assimilable form.

It will be observed, therefore, that livogen contains the two essential factors for normal blood formation—namely, liver extract and organic iron. For those particular cases of specific anæmias in which massive doses of iron are indicated iron ammonium citrate may be dispensed with livogen, the two products being in every way compatible.

Regarding the 'B' vitamins in livogen it is interesting to observe that results of recent scientific research have demonstrated that this complex also plays an important part in the process of regeneration of impoverished blood, and, in addition, it maintains appetite, promotes the proper action of the digestive tract including peristalsis, and sustains normal healthy growth. Thus the therapeutic value of livogen for the promotion of blood regeneration in all conditions of lowered vitality can be properly appraised by a study of its composition which is based upon the latest findings of research on the treatment of the various conditions arising from blood degeneracy.

USES

The principal uses for livogen in the ordinary course of everyday medical practice are in the treatment of the many conditions of weakness and lowered vitality of which a bad blood picture is a symptom. Examples of such conditions are those which accompany acute disease, the malaise following severe illness, weakness following a surgical operation and the form of depression which is so characteristic of influenza convalescence. Livogen is of value also as a general tonic in the many similar, but milder, conditions of lowered vitality, debility and lethargy which are met with almost daily in clinical practice; in such conditions the ingestion of livogen produces not only a reconstructive tonic effect upon the blood, but, by stimulating the appetite, it

renews vitality and hastens the return to normal health.

Livogen administration is remarkably beneficial also in cases of specific anæmias—both primary and secondary. In reporting on its value in these cases a physician in charge of an important hospital states that 'the severe secondary anæmias of various ætiologies.... respond exceptionally well to livogen exhibition.... it is quite the best treatment.... the effect is astonishing'.

Furthermore, in pregnancy and lactation, in febrile conditions and as a blood regenerator after severe hæmorrhage, livogen is of distinct value.

ADMINISTRATION AND DOSAGE

Livogen is highly palatable; it may be sipped neat from a wine glass, or taken in water, soda-water, or other suitable vehicle, preferably after food. It causes no gastric reaction, and it is acceptable to the most fastidious.

The dose varies from two teaspoonfuls to two tablespoonfuls per day according to the needs of the case, the average dose for an ordinary case of general debility and lowered vitality following illness being two teaspoonfuls once or twice daily.

It is a product of The British Drug Houses Limited, London.

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Original Articles

CARDIOVASCULAR AND OTHER MANIFESTATIONS OF EPIDEMIC DROPSY

By R. N. CHOPRA, M.A., M.D. (Cantab.)
LIEUTENANT-COLONEL, I.M.S.

and

S. C. BOSE, M.B. (Cantab.), M.R.C.P., D.T.M. (Lond.)

(From the School of Tropical Medicine, Calcutta)

WITHIN recent years epidemic dropsy has affected a large section of the population of the province of Bengal; its troublesome clinical manifestations and a fairly high mortality rate have attracted considerable attention, and much research has been carried out on this disease. The senior author (R. N. C.) during the last nine years has studied a number of epidemics in Calcutta. The majority of patients suffering from this condition, who came to the School of Tropical Medicine, Calcutta, for treatment, were admitted under his care into the Carmichael Hospital for Tropical Diseases and carefully studied. Thorough clinical examinations were made and the aetiological, pathological, bacteriological and biochemical implications were carefully investigated. The results of some of these observations have already been published. In this paper we propose to describe briefly the results of the studies of the patients who came under our observation during the latter half of last year. One of us (S. C. B.), who has extensive experience of cardiology in the tropics, studied these patients with regard to their cardiovascular changes. Any remarkable features in connection with this syndrome, which have come to our notice during these studies, have also been included in this paper. It is worthy of note that many striking features seen in the patients were typical of those occurring in acute specific infectious diseases such as measles, diphtheria, enteric fevers, etc., thus lending additional support to the views already expressed regarding its infective nature.

(i) *Incidence.*—It has been observed by previous workers that this syndrome shows a peculiar periodicity. In certain years, a widespread epidemic is met with, followed by a quiet period. These waves of morbidity are difficult to explain. This year, the seasonal rainfall has been excessive and the humidity has been abnormally high. The mean temperature has been more or less the same as in other years, and the method of storage of rice has not altered in any way, yet there have been hardly any admissions into the hospital and very few persons with this disease have come to the outpatient department even from Howrah, the notorious plague-spot from where most of the

Calcutta epidemics start. Some of the members of the staff of this institution, who were affected some years ago, and generally feel off-colour directly the season arrives, have had no recrudescence of unpleasant symptoms of their old malady. Each epidemic brings forth its own peculiarities and cases of one year greatly differ in severity, signs and symptoms from those of another year. The morbidity rate as well as the incidence of mortality vary enormously. In some epidemics the death rate is very high while in others it is exceedingly low. The epidemic of 1932 referred to in this paper was one of moderate severity, with a low mortality.

(ii) *Selection.*—Although all the members of a family are on exactly the same diet, the severity of symptoms varies enormously in different individuals. Children under five and persons over fifty either escape entirely or are only very slightly affected. This raises the question whether for each person there is a certain critical or absolute quantity of the noxious food-stuff ingested, beyond which symptoms arise, or perhaps the quantity of the noxious material is relative to the other articles of diet consumed. Very young children usually consume small amounts of the affected rice in comparison with milk, and we have not seen many patients under five years of age.

In a previous paper, Chopra and Basu (1930) found the maximum age incidence to be between twelve and seventeen years of age and that nearly all the patients were under thirty. The young adult belonging to this group usually consumes the largest quantity of rice, both absolutely and relatively in proportion to other food-stuffs. Old persons, however, eat less, and often have but one rice meal in 24 hours, so that the critical quantity is probably not reached, and they escape. Further, pre-existing diseased conditions of the gastro-intestinal tract such as amœbiasis, hepatitis of amœbic or malarial origin, bacterial and parasitic infections of the bowels and other conditions which lower vitality, increase the susceptibility of exposed persons. In our present series of cases such infections occurred in almost every patient. To ensure rational and successful therapy of these patients a thorough clinical examination is necessary.

(iii) *Clinical types.*—While cardiac involvement is the rule, its severity is not uniform. In certain epidemics, severe diarrhoea is the predominant symptom and the cardiovascular symptoms are of a mild nature. In patients with constipation, the cardiac features usually progress rapidly and become serious, often leading to a fatal end. In yet another group, mild cardiovascular symptoms are associated with a high rate of ocular complications such as glaucoma; there is as a rule only slight diarrhoea and œdema of the legs in these patients. Our belief that diarrhoea is produced by the toxic bases in the intestines which not only damage the capillaries and

produce œdema, but also produce exfoliation of the mucous lining of the gut, is further strengthened by the study of this series. The patients with advanced cardiac failure during the epidemic under review all recovered, except two, one a very old infirm and fat woman admitted *in extremis*, and the other a hopelessly anæmic girl of eighteen.

(iv) *Ætiology*.—The study of this epidemic and the series of cases discussed in this paper has further strengthened the views expressed by the senior author (Acton and Chopra, 1925) that epidemic dropsy and beriberi belong to a toxic group, where the three main signs are œdema, hypertrophy followed by dilatation of the heart, and peripheral neuritis. In epidemic dropsy usually only two of these signs are present, i.e., the œdema and the effects on the heart, and in dry beriberi there are cardiac lesions, marked peripheral neuritis, but little or no œdema.

This syndrome is produced by certain poisons elaborated in food which is improperly stored. Beriberi has been produced by rice or by the exclusive use of tinned provisions, and living on a diet mainly consisting of dried fish is said to have produced an epidemic in Labrador. It is well known that, provided proteins or amino-acids are present, the decomposition of these substances to toxic products is not the exclusive property of any particular protein or any particular species of bacterium. All cases of epidemic dropsy seen by us occurred among those whose main dietary consisted of rice and in almost every case it was established that the rice was diseased. A spore-forming proteolytic bacillus of the *vulgatus* group is commonly found in the diseased grain (see table of cases). In this connection it may be mentioned that Bernard of Saigon found a very similar bacillus and described an infection occurring in animals when fed on these bacilli. We have further confirmed our previously enunciated views that there is no close connection between avitaminosis and this disease, because if this were the case it would occur in an epidemic form when associated with famine conditions and this certainly has not been so in Bengal. The findings of Acton and Chopra (1927) regarding this bacillus occurring in the urine and stools of patients were confirmed in a number of other cases. Toxins elaborated by this organism resemble histamine in having a powerful effect on the capillaries.

Physical signs and subjective symptoms

Dyspnœa.—This is an early feature, complained of before gross evidence of cardiac damage appears (see table of cases). At first it is a quick and shallow hyperpnœa of the type seen in some anæmic states. It is either mild and constant, or spasmodic, often being worse at night. As the mechanism is obscure, the following discussion

may be of interest. This primary hyperpnœa may be explained entirely by local lesions, i.e., by the turgid capillaries encroaching on the alveolar spaces and diminishing the calibre of the terminal bronchioles. Next we suspect some anæmia of the respiratory centre caused by the 'capillary crisis' elsewhere; the resulting anoxæmia would stimulate the centre to increased respiratory movements. Finally, cardiac failure with congestion supervenes and a CO₂ excess is added on to the oxygen-want. The patient with orthopnœa is not cyanotic but has an ashy pallor, called pallid asphyxia, which is almost a terminal feature.

Edema.—This occurs to a greater or lesser extent in all cases (see table). The condition, as met with clinically in anæmic states and in cardio-renal disease, is characterized by excess of fluid in the subcutaneous tissue spaces and is recognized by the affected part being pale, painless and pitting on pressure. We now know that two other conditions coexist with subcutaneous œdema and even ante-date its appearance, namely, general hydræmia and some excess of fluid in the tissue spaces of the skeletal muscles also. The existence of these two states is suggested by an increase in weight of the patient, and clinically obvious œdema can be predicted to occur after a few days of the above finding. The initial œdema of epidemic dropsy is quite distinctive in that it is of the solid type, and the affected skin is dusky-red, hot and tender on pressure, and it affects the skeletal muscles, heart and possibly the viscera. This swelling consists of two components, a small amount of transudate and a network of turgid capillaries. The hot flush is similar to an erythema, but differs in its darker colour, presumably on account of a poorer oxygen-content caused by stasis. Curiously, the stasis never reaches the degree to produce a cyanotic hue. With advanced cardiac failure, the œdema increases in amount and the skin pits more readily on pressure. It would be interesting to record the lower-limb volume in the various stages of the disease, whichever way it may terminate and to compare these figures with the total body-weight on the same dates.

The patient complains that his legs no longer carry him, but that he has to carry his legs after him.

The typical initial œdema is not strictly confined to the legs but may extend up to the root of the neck. The skin in facial or ocular œdema, however, is never of the red, hot type; but it is pale.

Anæmia is a prominent feature in all cases. Leaving aside other coexisting causes, such as parasitic anæmia, its degree is proportionate to the rate at which the malady progresses and to the more advanced degree of cardiovascular damage and heart failure. Even within the first

two or three days of the onset in most cases, a marked pallor of the face and mucous membranes is very distinctly noted. Other observers have found a moderate degree of hydræmia coexisting with œdema, as evidenced by a low specific gravity of the blood, and a low ratio of corpuscles to plasma. This hydræmic type of anæmia is revealed by a low hæmoglobin value with an erythrocyte count not lower than 3 or $3\frac{1}{2}$ millions per c.mm. Later in the disease, the anæmia may perhaps be explained by capillary hæmorrhages or by inhibition of the erythrocyte production due to the deleterious action on the hæmatopoietic system by the toxins absorbed from the gut. The main reason of facial pallor and anæmia in the early stages is probably the widespread capillary dilatation which produces capillary stasis all over the body and particularly in its lower half. This necessarily curtails the amount of blood in actual and active circulation. The arterioles and venules which lie above the level of the base of the heart are poorly filled and so pallor thereby results. Clinically, the anæmia seems more severe than the count of red blood corpuscles and the hæmoglobin value show.

Blood pressure.—Though in our previous paper the occurrence of high systolic readings has been noted, the unanimous finding in all well-established cases is a low systolic reading, rarely exceeding 110 mm. and a very low diastolic pressure of 50 mm. of mercury or less (see table of cases). This low mean blood pressure is fully in accord with the widespread capillary dilatation throughout the body.

Cardiovascular system.—When the invasion of a malady is heralded by prominent cardiac symptoms and signs, which rapidly get worse and often lead to a fatal issue, it is natural to concentrate on the myocardium as the seat of damage. One recalls the cardiac crises in diphtheria and enteric fever and expects to find in epidemic dropsy similar histological changes to those found in the above two diseases. But to one's disappointment the heart muscle, in even the worst cases of epidemic dropsy, shows neither inflammation, degeneration nor hypertrophy. Acton and Chopra (1927) were the first to study the histology of an epidemic dropsy heart. They described the increased vascularity of the myocardium, so that the smallest capillaries were readily seen. Besides the increased vascularity, œdema had separated the muscle fibres which themselves showed no changes. Later Shanks and De (1931) confirmed these findings, and found that the only remarkable change was a wide network of dilated capillaries separating the individual muscle fibres. It appeared as if the muscle fibres were being pressed upon from all sides by the dilated capillaries. These changes were uniformly spread throughout the right and left ventricles and there were no indications that the capillaries were more numerous or more densely packed in

the left ventricle than in the right. From these data no evidence can be adduced in favour of the popular conception of epidemic dropsy being a condition due to left-heart failure as contrasted with beriberi which is considered as a condition produced by right-heart failure. Further, Sir Thomas Lewis and other cardiologists do not endorse the old conception of dividing heart failure into two separate types, i.e., those due to left-heart and right-heart failure, respectively. The conception at present accepted is the division of heart failure, very broadly, into two types, namely, failure with venous congestion, and failure with anginal pain. It would therefore be reasonable to regard the heart failure in epidemic dropsy as being that of the congestive type.

The essential histological changes seen in the whole of the cardiovascular system are a very widespread capillary dilatation and stasis throughout the body but most marked in the dependent parts. Similar histological changes are seen in the epicardium and in between the muscle fibres of the myocardium throughout the ventricles and the auricles. There is no evidence of a cellular infiltration or proliferation around the capillaries or elsewhere. The muscle fibres, so far as can be made out, are perfectly normal in appearance. The toxins apparently have a special affinity for the capillary endothelium which they damage leaving the other cells untouched. It is therefore permissible to pause and consider if our previous conception of an essential primary cardiac failure should not be modified, and whether this widespread capillary dilatation and stasis of the whole circulation may not play the leading rôle in the onset and progress of cardiac failure. In short the true cause would appear to be an all-round circulatory failure accentuated by myocardial weakness and not a primary cardiac failure. It is well known that capillary dilatation with stasis beyond a certain degree will accommodate such an enormous quantity of blood that the big veins, the chambers of the heart and the larger arteries will become half empty, and circulation will be brought nearly to a standstill. In cases of advanced aortic regurgitation the arteries and dilated arterioles are poorly filled and therefore patients suffering from aortic disease tend to show pallor. Further, the heart failure in aortic regurgitation is rapidly progressive and ends fatally without much evidence of back pressure, venous stasis and congestion of the systemic veins. Cyanosis is exceptional even towards the end, in cases of advanced aortic regurgitation. According to Lewis, in all cases of advanced aortic regurgitation, there coexists a well-marked dilatation of the smaller arterioles and capillaries and it is the latter event which produces the typical Corrigan's or water-hammer pulse with a very low diastolic pressure. On account of the free leakage through the aortic valves, a large volume of the blood permanently

stagnates in the capacious distended left ventricle, which however takes no part in the active circulation. The associated dilatation of the arterioles locks up some more blood.

In the fulminating type of heart failure in epidemic dropsy the clinical picture is very similar to the above, and such signs and symptoms as well-marked suprasternal pulsation, pulsating carotids, a water-hammer pulse of low tension and a low diastolic pressure are present. In acute epidemic dropsy therefore we may conceive of a similar mechanism whereby the patient bleeds into his own distal capillaries; large quantities of blood thus stagnate in the capillaries and are cut off from taking part in the circulation. The contractile power of the left ventricle is too poor to drive the increased volume of the stagnant capillary blood to the veins and back to the right heart. Consequently the heart as a whole is badly filled and badly emptied. The coronary circulation depends for its integrity on an adequate systolic output from the left ventricle and a relatively high 'head of pressure' beyond the aorta. Both these factors thus suffer in epidemic dropsy and a certain amount of coronary starvation is rendered probable.

From our clinical experience in epidemic dropsy we would classify the diseased hearts into three well-marked clinical types:—

- (a) Acute, or fulminating: here the patient has the heart affected at the very start, failure progresses and death may occur within four to seven days. These cases resemble the picture of an acute left-heart failure. This type, with a high mortality, was common in the epidemics of 1926 and 1927.
- (b) Subacute or chronic: here the heart is less rapidly affected, and failure, from which recovery is usual, is a slow process. These cases resemble the picture of a combined right- and left-sided failure, with slight cyanosis, jugular distension and general systemic venous congestion. Our present series of cases fell under this group.
- (c) *Formes frustes*: here the heart either wholly escapes, or is very slightly affected. This type was seen in one previous year.

The existence of these three distinct types cannot be explained in terms of the varying degrees of histological changes in the heart wall itself. But it is easy to understand the mechanism of these three modes of cardiac failure, by recalling the picture of a general capillary dilatation. The degree and severity of circulatory failure along with a secondary cardiac weakness is directly proportionate to the degree and extent of capillary dilatation that exists. The acute fulminating type of failure starts with a very deep and extensive capillary

distension and stasis, somewhat similar to that in surgical shock or acute histamine poisoning. The blood is locked up in the capillaries, and thus is side-tracked from the circulation. Consequently the veins, the heart and big arteries are relatively empty, and sudden syncope and death may result. When the supply of fuel is cut off, the engine cannot continue its work. Clinically, these cases die neither showing cyanosis, jugular distension, a passively congested liver nor any distal œdema of passive congestion. Next, in the subacute or chronic type, a lesser degree and extent of capillary distension occurs and the veins and the right heart are better filled. Some venous stasis in the systemic circulation and right heart is obvious. In general, the more delayed the onset and the progress of failure, the more likely is the clinical picture to resemble a typical right-sided failure, and this is what we find in all our present series of cases. We are able to show a new orientation in our conception of the mechanism of the cardiac failure if we merely recall the essential morbid histology. What was previously called an acute left-heart failure is probably a condition of over-filled and multiplied capillaries, with a relative emptiness of the big veins of the right or left heart, a starved coronary circulation and half-empty large arteries. What was formerly called a right-sided failure, and which we do find in the more chronic types, is probably a condition of moderate capillary engorgement, an over-filled venous system and right heart, with comparatively less blood in the left heart and arteries.

We have briefly described the mechanism and the mode of progress of the cardiovascular disturbances in epidemic dropsy, which consist of cardiac failure of the congestive type aggravated by vascular disturbances in the peripheral circulation. The process of clear thinking is very materially assisted by the use of exact terms and we suggest that the typical damage and defects may be expressed as a 'cardio-capillary crisis'. Cardiac failure has been very tersely defined by Lewis thus: 'It signifies inability of the heart to discharge its contents adequately; and this failure culminates in manifestations with which we are all familiar, namely dilatation of the heart, general venous congestion and dropsy'. The 'capillary crisis' consists of an absolute lack of tone and resiliency of the distended walls of the capillaries whereby the blood, instead of being further propelled along to the venous system, stagnates and behaves as a useless but harmful dead weight to the process of circulation. As the cardiac failure progresses, the increasing dilatation of the right heart is reflected on to the big veins and then to their finer tributaries. As the left heart dilates and mitral incompetence and regurgitation eventuate, there is a relative emptiness of the aorta and of the whole arterial tree. To sum up the events in chronological order,

we start with the initial toxic capillary dilatation followed by cardiac failure, arterial emptiness and venous fullness. In left-sided cardiac failure, the aorta and arterial tree are but poorly filled; this results in oligæmia of the whole arterial tree and a relative starvation of the coronary circulation to the myocardium itself. In the acute fulminating type, this arterial emptiness is incompatible with life, there is no time for evidence of right-heart failure to appear, nor is there sufficient blood left over by the dilated capillaries to over-fill the venous system. In the more chronic types, however, the clinical picture is that of a typical back-pressure type of heart failure superimposed on the initial 'capillary crisis'.

Heart

Physical signs.—For the benefit of those who are not likely to meet with this condition in their practice, we would like to point out that, in the whole range of clinical medicine, we know of no other acute specific febrile malady where a perfectly strong and healthy lad or a young adult may be struck down within two or three days, with the fully-developed picture of an acute congestive type of cardiac failure. There is no other disease where, so early, the full fury of the onslaught is concentrated on the entire cardio-capillary system. In extreme cases, the acutely progressive congestive failure resembles the left-heart failure that is seen in the terminal stages of syphilitic heart disease with aortic regurgitation. And yet, post mortem, there is hardly any naked-eye or conspicuous histological change in the pericardium, myocardium or endocardium. In the milder intoxications, the heart failure resembles that in grave myocarditis. In children who remain alive for more than 4 to 6 weeks, the type of failure closely resembles that seen in mitral affections of rheumatic origin. True muscular hypertrophy, however, has not been met with in the few cases on which post-mortem examinations have been done, nor has any valvular or mural endocarditis been found.

In describing the clinical features we propose to adopt the classical scheme of Sir Thomas Lewis, namely, congestion, enlargement, valves, rhythm, infections, ætiology and vessels.

Congestion.—The typical signs are, marked fullness and pulsation of the jugular veins, enlarged and possibly pulsating liver, œdema of the legs, some general anasarca, and even ascites and hydrothorax. In the very acute cases, however, the systemic veins are not markedly engorged, only the lungs showing very early passive congestion and œdema. There is neither muscular hypertrophy nor any valve disease. This congestive failure furnishes yet another proof of the hollowness of the traditional theory of 'broken compensation' as the cause of a failing heart. Cyanosis is rare, except in those patients with a terminal broncho-pneumonia.

The initial pallor of the face and lips may progress to a pallid asphyxia, which is an ominous sign.

Enlargement.—The apex is usually displaced downwards and outwards, often in the 6th interspace beyond the anterior axillary line. The cardiac impulse is diffuse and wavy, as in the over-acting heart of dilatation. The left border is palpable outside the nipple. The upper margin of cardiac dullness reaches up to the 2nd costal cartilage, and a small patch of dullness is noted over the 2nd left costal cartilage and interspace near the edge of the sternum. Beneath this patch of dullness, distinct pulsation may be seen and felt, and on orthodiagraphy this appears to be the dilated pulmonary artery.

Valves.—These are never diseased. Abnormal cardiac sounds and bruits are heard and though they have lost their former pride of place, in modern heart work they have at least an academic interest. The first sound is short, sharp, toneless, and resembles so nearly the second sound that, with tachycardia, the heart sounds are almost 'tie-tie'. The most important organic bruit is that heard over the apex, systolic in time, conducted to the axilla and which partly or wholly replaces a weak first sound. Tradition holds this to be caused by a leak of the mitral valve and we regard it as such, since the heart is enormously dilated and a slack mitral ring is probable. But we wish to stress the importance of another systolic bruit that is heard over the pulmonary area, which has hitherto been neglected as being merely a hæmic or a functional affair. If one must consider bruits at all, a place of honour must be found for this probably pulmonary systolic murmur (see table of cases). Most decidedly it is the earliest to appear, it is constant in all postures and phases of respiration and is harsh and loud; it entirely replaces the first sound, and is the last bruit to disappear on recovery; indeed it may never fully disappear. We must consider this pulmonary systolic murmur in relation to the pulsation and dullness over the 2nd left costal cartilage and interspace, to be produced by a dilated pulmonary artery. The term 'hæmic or anæmic bruit' is a misnomer, and must be finally discarded, because a merely qualitative change in the blood is quite unable to produce a bruit. All bruits owe their origin to the same laws of physics, namely, the production of a 'fluid vein' whose vibrations are audible. We know that a fluid vein can only be produced if there is a relative change in the calibre of the orifice and the diameter of the exit tube. The blood must either pass through a constricted orifice, or pass out into a dilated chamber before a fluid vein can be formed and an audible murmur heard. We know that in epidemic dropsy, as the pulmonary capillaries are also dilated and engorged, the strain must fall on the main pulmonary artery, whose wall not being as firm and elastic as that of the aorta,

easily gives way and a dilated pulmonary artery is the result. Epidemic dropsy therefore impairs the integrity of the whole arterial system and we should regard the pulmonary systolic bruit as an expression of the widespread arterial damage in the pulmonary circuit. Further, the aorta is not spared. A well-marked supra-sternal and carotid pulsation along with a low systolic and diastolic pressure points to the same weakness of the wall of the aorta and carotid arteries. Finally, venous pressure is increased and, thus, no part of the cardiovascular system escapes injury in this disease. If we get this picture clearly fixed in our minds, we shall the better grasp the manifestations of this syndrome.

Rhythm.—Tachycardia is constant, with rates varying from 110 to 130 and rarely exceeding 140 per minute, and it is out of all proportion to the pyrexia. Other things being equal, the increased heart rate is a measure of the severity of the cardiac failure. Pulsus alternans is occasionally present. Towards recovery, an occasional extra systole may develop, and, later still, a sinus arrhythmia. While the A—V bundle of His may be irritable and conduction time quickened, there is never any delay or block of the main bundle or its branches.

Pulse.—A fall of blood pressure is the rule, including both systolic and diastolic. The diastolic reading falls to 30 mm. of mercury or even less, producing the water-hammer or Corrigan type of pulse of aortic leak. The arteries possibly develop a weakness of the walls but there is no arteritis, and the veins are over-filled in congestive failure. The capillaries, we have already stated, are markedly dilated so that the affected tissue looks angiomatous or hæmorrhagic from a distance. Occlusion or rupture of the vessels is a rarity. The typical pulse is soft, small, rapid and of low tension.

Heart: Late sequels.—While recovery from the acute attack is usual, the affected patients have a difficult future to face, especially those who have had the heart and capillaries badly affected. All these patients have ominous symptoms of a relapse as soon as they eat the affected rice of an epidemic year and are the first to become ill; it seems as if they had become permanently sensitized to the toxin. Leaving aside the bad years the majority of adults over thirty years of age confidently state that they are never the same again; they are easily susceptible to palpitation of the heart and swelling of the feet and have less than their usual capacity for exertion, as if a permanent loss of cardiac reserve had come about. Athletic younger men also complain they have not the same physical stamina as before. This condition is hard to explain because we have no evidence of permanent structural damage to the myocardium. We know, of course, that a severe attack of enteric fever, influenza or bacillary dysentery also frequently produces a permanent loss of cardiac

reserve, where also we have no proof of a permanent structural lesion in the myocardium, but, arguing by analogy, we may regard this as a definite fact. Yet, a real danger is lurking here. Ever since the epidemic of 1909 and 1910, this fact has been so much over-stressed that it has become almost an obsession with the patient and his doctor. Even to-day, people suffering with their hearts walk into the consulting room, place their diagnosis on the table and ask for the specific remedy. Frequently the patient is not carefully examined and is dismissed, well pleased with the advice, on calcium therapy and a rich vitamin diet. The true condition in elderly persons may be a syphilitic, a hypertensive, or a renal heart, a condition most dangerous to overlook. Far better is it to judge the case on actual physical signs than to pay too much attention to the history. These warnings are sounded as a result of experience with cardiac cases in Calcutta.

Blood.—The blood on venesection is very striking to the naked eye. The colour is dark chocolate instead of dark red: it clots almost at once; the clot is softer and more gelatinous; and the serum is bile-tinted. This is quite unlike the blood in uræmia or chronic heart failure.

Other manifestations

Fever.—Rise of temperature is an initial and fairly constant symptom and its degree is a rough measure of the severity of the illness, but with one possible exception (*see table*). Where diarrhœa is very severe and loss of body fluids extreme, a sub-febrile state is seen, although the illness is truly grave. Another feature is quite distinctive and unique. In no other disease do we find such a persistent difference in the temperature of the skin of the legs, as compared to that of the face. It would form a most interesting study to make simultaneous and serial observations of the temperature in different parts of the body, such as the skin of the legs, face, and axilla, and to check these readings with the rectal temperature. The dusky-red hot legs typical of the disease show these changes less markedly as the condition improves, until finally the leg temperature agrees with the general body temperature elsewhere. The erythema fades and may be replaced by a darkish pigmentation of the affected skin.

Diarrhœa.—In an earlier epidemic, diarrhœa was the exception and the cardiovascular system was so severely affected that a very high mortality was seen as early as the first week. This is explained by the absence of elimination and the locking up of the toxins. A moderate diarrhœa of about four to six motions a day is not so ominous. The other extreme, approaching the algid type with loss of body fluids, is of serious omen. The initial toxic diarrhœa is often the starting point of the malady and the typical Gram-positive bacilli are frequently met.

with. These were only detected in three patients of this series. The reason is probably that the majority of the patients came in for treatment when the disease was well developed. At this period probably other varieties of intestinal flora get the upper hand, overrun the typical rice bacilli and make them difficult to detect. This would explain our not finding them in all the samples examined and we would therefore stress the importance of immediate and repeated stool examinations at the very onset of the malady. Acton and Chopra (1927) frequently found in the stools of epidemic dropsy patients, when examined early in the disease, these Gram-positive bacilli, whilst in the controls the majority of organisms were Gram-negative bacilli with the ordinary Gram-positive cocci.

Knee jerks.—In typical beriberi, the knee jerks become exaggerated at first, but later diminish and may entirely disappear. Inflammatory changes in the nerves have been demonstrated in such cases. A perusal of the table of cases under review shows a similar state of affairs, though perhaps not to the same extent. In some patients the knee jerks were definitely exaggerated while in others they were markedly decreased, and this was also our experience in the other epidemics we have studied previously. There is thus undoubted evidence of the presence of neuritis in epidemic dropsy.

Treatment.—The lines of treatment adopted in our present series were the same as those used by Chopra and Basu (1930). Rice was entirely cut out from the dietary. It was definitely established that the progress was much slower if rice was allowed as a part of the diet. We have seen many instances of patients who, while under treatment, secretly took rice and had a relapse of all the signs and symptoms.

Diarrhoea, if mild, needs no treatment but if severe 15 to 30 minims of liquor ferri perchloridi are distinctly helpful. When there were signs of cardiac failure administration of digitalis and digitalis-like substances again proved a failure. From the discussion of the pathological changes met with in the heart it is obvious that digitalis can do little good when the muscle fibres of the heart are normal and are being pressed upon by fluid. Any drug, which might act on the small arterioles and capillaries and restore their tone and thus decrease the fluid pressing on the muscle fibres, ought to produce beneficial results. Adrenalin would bring about such a state of affairs and daily intramuscular injections of 2 to 4 minims of 1 in 1,000 solution considerably improved the condition of the patients. Unfortunately a sensitiveness to this drug develops after it has been given for a few days consecutively, and palpitation and a feeling of oppression in the chest are so distressing that the patient refuses to have the drug.

We have obtained good results with 20 to 30 minims of tincture of ephedra administered two

or three times a day either by itself or in combination with a little iron and strychnine. Ephedrine acts in very much the same way as adrenalin, its action being not so powerful but more prolonged. Further, large quantities of pseudo-ephedrine contained in the Indian ephedras have a marked stimulant action on the myocardium and the combined action of the two alkaloids makes this preparation a very useful remedy in the treatment of epidemic dropsy. Ten grains of calcium lactate two or three times a day if combined with the above treatment help in those patients where, on account of diarrhoea, there is a considerable drain of fluid from the body.

Discussion

Our discussion will be as brief as possible. The first thing is to discard, for the moment, all hypotheses which tend to obscure the issue and then to sum up all the known facts of ætiology, pathology and symptomatology: to endeavour to trace the path of intoxication and locate the habitat and destiny of the suspected toxins: finally, to build up a rational scheme of prophylaxis well understood by laymen, and a plan of therapy easily carried out by practitioners.

The ætiological factors require no further emphasis beyond the fact that our recent work tends to indicate the Gram-positive bacillus as the source of toxins partly formed outside the body and ingested as chemical poisons, and partly manufactured in the human gut. The pathological findings may be accepted as being the result of the disease, and not the remote effects of other mixed and secondary infections. A study of the pathology of the living indicates a 'cardio-capillary crisis' as being the most serious condition present, which leads to progressive heart failure and, occasionally, to death.

The path of intoxication starts with the ingestion of the affected rice. In the stomach and duodenum local irritation is produced which may proceed down to the rectum, causing areas of congestion and necrosis of the mucosa. Local injury to the rectal mucosa causes occasional vascular swellings which bleed profusely. The absorption presumably takes place through the liver which also shows the typical lesions and the antitoxic function of the liver is severely tested but fails, and finally the toxin reaches the general circulation. Although symptoms may commence as early as twenty-four hours after feeding, the effects of this intoxication are very severe and serious and may continue for some weeks after a rigid stoppage of the suspected food-stuff. This suggests a massive storage of the toxins, or a linkage with the cells of various tissues, such as is known to occur in heavy-metal poisoning, with lead or mercury, for example. Possibly the liver and the glands of secretion all along the bowel wall may be the

storage organs. The digestive juices and bile may be the medium whereby a daily dose is constantly released into the duodenum and thus the gastro-intestinal disturbances persist. The mechanism for destruction or neutralization of these toxins in the body is slow in action, if it does exist at all. The elimination takes place by the bowels and kidneys although evidence of an unnaturally toxic urine being passed is not forthcoming. We have seen cases relapse after an initial improvement and this can only be explained by supposing that, at times, a massive dose of this locked-up toxin is released into the general circulation and renders the 'cardio-capillary crisis' as bad as ever. Rational therapy might be summed up as follows:—

1. Stimulate elimination of the toxins by the bowels.
2. Neutralize or break down the toxins in the bowels into inert harmless products.
3. Prevent absorption of the toxin.
4. Stimulate the antitoxic power of the liver so that the toxins are broken down into simpler products.
5. Stimulate the defensive mechanism of the body whereby the ductless glands may produce hormones destructive to the toxins.
6. Quicken up the process of elimination by the kidneys.
7. Add to the diet, appropriate vitamins which may render the toxins inert.
8. Counteract the 'capillary crisis' throughout the body and thus hasten the process of circulation.
9. Support the heart by tonics.
10. Relieve the venous congestion by leeches or venesection.

In practice, however, all these ten points cannot be dealt with for want of exact knowledge but the prospect is far more

hopeful than might at first sight appear. We have, in the past, relied exclusively on cardiac tonics, in one or other shape, and have ignored the other vital therapeutic points. Since the heart is 'sinned against as well as sinning' this narrow view of therapy could not possibly give the best results. The 'cardio-capillary crisis' is best dealt with by that group of drugs which has a sustained vaso-pressor effect, combined with the power to counteract the increasing permeability of the minute capillary walls. It is fortunate that in ephedrine we possess a potent remedy whose optimum and selective seat of action is in the capillaries, and an extended use of ephedrine has fully confirmed the success which seemed likely. The digitalis group of drugs has failed us, because this capillary crisis is left untouched and until this is corrected no cardiac tonic can maintain adequately the circulatory process. In calcium we possess a means of decreasing the permeability of the capillary walls.

In a subsequent paper we hope to give a detailed analysis of all the epidemics that have been studied by the senior author during the past nine years.

REFERENCES

- Acton, H. W., and Chopra, R. N. (1925). The Problem of Epidemic Dropsy and Beriberi. *Indian Med. Gaz.*, Vol. LX, p. 1.
- Acton, H. W., and Chopra, R. N. (1927). Further Investigations into the Aetiology of Epidemic Dropsy. *Indian Med. Gaz.*, Vol. LXII, p. 359.
- Chopra, R. N., and Basu, U. P. (1930). Cardio-vascular Manifestations of Epidemic Dropsy. *Indian Med. Gaz.*, Vol. LXV, p. 546.
- Chopra, R. N., Dikshit, B. B., and Pillai, K. V. (1929). Comparative Action of Ephedrine and Pseudo-ephedrine on the Heart. *Indian Journ. Med. Res.*, Vol. XVI, p. 780.
- Shanks, G., and De, M. N. (1931). Pathology of Epidemic Dropsy. *Indian Journ. Med. Res.*, Vol. XIX, p. 469.

Table of cases

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
1	M., M., 24, œdema, legs, 2 weeks; dyspnœa 1 day; similar cases in neighbourhood. Shibpore—6 years.	Jugular veins mod. full; liver engorged, exercise (10 hops) raised heart rate from 80 to 96 producing no dyspnœa, rate falls to 80 within 2 minutes. Apex—5th and 6th interspaces $4\frac{1}{2}$ inches out; 5th rib lifted up with systole, left border palpable indicating definite hypertrophy; systolic bruit at pulm. area only. $\text{B.P. } \frac{100}{55}, \frac{P}{R} = \frac{80}{20}$	Gram-positive large diplococci. Trichuris ova. Iron, mag. sulph., tr. ephedra. Cured.
2	I. Ch., M., 27, œdema, tenderness, legs, 18 days; dyspnœa 3 days; similar cases in	23-3-32. Slight congestion in eyes, liver slightly engorged, apex 1 inch away from nipple,	Trichuris ova. Iron, mag. sulph., strychnine, digifortis, tr. ephedra,

Table of cases—contd.

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
	neighbourhood. Calcutta—4 years. (Disease started as diarrhoea which lasted for a day only; with the stoppage of diarrhoea the œdema of the legs appeared.)	systolic bruit loudest at the pulm. area. B.P. $\frac{88}{30}$ $\frac{P}{R} = \frac{120}{24}$ 2-9-32. General improvement. B.P. $\frac{100}{40}$ $\frac{P}{R} = \frac{100}{24}$ 21-9-32. General improvement, but liver engorged to the same degree; systolic bruit maximum in pulm. area. B.P. $\frac{102}{50}$ $\frac{P}{R} = \frac{88}{24}$	pituitrin, adrenalin, blood letting, leeches, potass. brom. Left hospital on own responsibility.
3	H., M., 5, generalized œdema, 2 weeks, preceded by fever for 4 days; rash on feet, solid type of œdema in legs; a few other family members affected; dysentery 6 months back. Barasat—all along.	Advanced congestive failure; jugulars, liver, lungs engorged; marked suprasternal and carotid pulsation; apex 6th and 7th interspaces beyond ant. axillary line; systolic bruit harsh and loudest over pulm. area; also typical mitral systolic over apex; short sharp first sound; mitral incompetence. B.P. $\frac{85}{40}$ $\frac{P}{R} = \frac{132}{40}$ 9-9-32. General improvement; liver $\frac{1}{2}$ inch smaller, right lung base congested; apex 5th interspace and $\frac{1}{2}$ inch less out; systolic bruit softer in all areas, but loudest over pulm. area. B.P. $\frac{90}{40}$ $\frac{P}{R} = \frac{116}{36}$	Gram-positive organisms (mostly staphylococci), yeast. B.T. 10 days after admission. Iron, strychnine, digifortis, atebria. Cured.
4	H., M., 2, fever, œdema, legs, one week; diarrhoea; rash, on both legs; a few other family members suffering from similar complaint; dysentery 6 months back. Barasat—all along.	26-8-32. Advanced congestive failure; jugulars, liver, lungs engorged; marked suprasternal and carotid pulsation; apex 6th interspace beyond ant. axillary line; systolic bruit harsh and loudest over pulm. area; also typical mitral systolic over apex; short, sharp, first sound. B.P. $\frac{80}{33}$ $\frac{P}{R} = \frac{124}{18}$ 9-9-32. Slight general improvement; liver $1\frac{1}{2}$ inches smaller; right lung base congested; apex 5th interspace and $\frac{1}{2}$ inch less out; systolic bruit in pulm. area only. B.P. $\frac{80}{30}$ $\frac{P}{R} = \frac{100}{40}$	
5	H., M., 7, œdema, legs, 3 weeks; fever 2 weeks; rash, legs; a few other family members suffering; malaria several attacks; dysentery 6 months ago; legs tense, red and glossy; loss of knee jerks. Barasat—all along.	23-8-32. Liver slightly engorged; apex 1 inch away from nipple; systolic bruit loudest at pulm. area. B.P. $\frac{88}{30}$ $\frac{P}{R} = \frac{120}{24}$ 2-9-32. General improvement. B.P. $\frac{100}{40}$ $\frac{P}{R} = \frac{100}{24}$ 21-9-32. General improvement; systolic bruit maximum in pulm. area. B.P. $\frac{102}{50}$ $\frac{P}{R} = \frac{88}{24}$	Gram-positive organisms. (No Gram-positive spore formers.) B.T. 10 days after admission. Iron, strychnine, tr. ephedra, mag. sulph., atebria. Cured.

Table of cases—contd.

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
6	H., M., 32, fever 3 weeks; œdema, legs, palpitation, dyspnoea 2 weeks; erythematous rash (both legs); a few other members of the family suffering; dysentery 4 months ago; malaria in the past; knee jerks exaggerated (left more than right).	2-9-32. Liver, lungs engorged; jugular and suprasternal pulsation; apex 1 inch outside nipple; systolic bruit loudest in pulm. area. B.P. $\frac{105}{65}$, $\frac{P}{R} = \frac{88}{18}$ 21-9-32. General improvement. B.P. $\frac{105}{65}$, $\frac{P}{R} = \frac{84}{20}$	Gram-positive spore formers, morphologically similar to <i>B. vulgaris</i> . Agglutination against <i>B. vulgaris</i> (isolated from his own stool)—negative. Iron, strychnine, tr. ephedra, mag. sulph. Cured. He was admitted on 1-9-32 and discharged on 16-9-32. He went out but came back with palpitation. Palpitation became severe and he had to be propped up. He was cured of the symptoms after about 2 weeks and was discharged on 30-9-32.
7	H., M., 4, fever followed by œdema legs—12 days; dyspnoea off and on, rash, loose bowels in the beginning; a few other members suffering; several attacks of malaria; dysentery 6 months ago. Barasat—all along.	23-8-32. Marked venous congestion; jugulars full, pulsating; liver, lungs engorged; carotid and suprasternal pulsation; apex 6th interspace beyond ant. axillary line; right border dullness is 1 inch right of sternum; harsh systolic bruit loudest in pulm. area; typical mitral systolic over apex; mitral regurgitation. B.P. $\frac{96}{40}$, $\frac{P}{R} = \frac{140}{48}$ 9-9-32. Improved; carotids, jugulars pulsating; bruits in all areas. B.P. $\frac{95}{40}$, $\frac{P}{R} = \frac{116}{40}$	Single colony of Gram-positive spore formers, morphologically similar to <i>B. subtilis</i> . Agglutination against <i>B. vulgaris</i> (isolated from No. 6)—negative; Gram-positive organisms (mostly cocci). Iron, strychnine, quinine. Cured.
8	H., F., 24, œdema, pain legs 2 months; dyspnoea; knee jerks; right normal, left exaggerated; several members in the family suffering from similar complaints. All along in Barasat.	23-8-32. Carotid, suprasternal pulsation; apex—5th interspace, $4\frac{1}{2}$ inches out; harsh systolic bruit in all areas, loudest at the pulm. area; first sound short, sharp, mitral leak. B.P. $\frac{90}{50}$, $\frac{P}{R} = \frac{120}{40}$ 21-9-32. General condition much improved; systolic murmur in pulm. area only. B.P. $\frac{105}{60}$, $\frac{P}{R} = \frac{92}{24}$	Gram-positive organisms (mostly cocci); single colony of Gram-positive spore formers. Agglutination against <i>B. vulgaris</i> (isolated from No. 6)—negative. Iron, strychnine, pandigal. Cured.
9	H., M., 2, fever followed by diarrhoea, slight œdema feet (evening) 1 week, scabies; many other family members suffering from similar complaint; dysentery 6 months ago. Barasat—all along.	26-8-32. Suprasternal and carotid pulsation; apex—5th and 6th interspaces beyond ant. axillary line; systolic bruit loudest at pulm. area; typical mitral systolic over apex; first sound short and sharp; mitral regurgitation. B.P. $\frac{70}{30}$, $\frac{P}{R} = \frac{120}{40}$ 9-9-32. General improvement; apex—same position; murmur still loudest over pulm. area. B.P. $\frac{80}{40}$, $\frac{P}{R} = \frac{40}{R}$	B. T. (day of admission) very scanty Gram-positive organisms. Iron, strychnine, quinine. Cured.

Table of cases—contd.

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
10	A. I., F., 34, œdema legs, palpitation, dyspnoea, vomiting 2 months, glossy and tender legs; knee jerks right—exaggerated, left—normal; as a rule constipated, but had 3 diarrhoeic stools within last 16 hours; husband had œdema feet, and died one week ago. Present residence, Calcutta .. Previous residence, Asansol (20 years).	31-8-32. Orthopnoea; jugulars full; carotid and suprasternal pulsation; apex—6th interspace, 5½ inches out; systolic bruit maximum in the pulm. area. B.P. $\frac{130}{70}$ $\frac{P}{R} = \frac{112}{40}$ 5-9-32. B.P. $\frac{138}{75}$ $\frac{P}{R} = \frac{120}{40}$ 9-9-32. Worse, broncho-pneumonia. B.P. $\frac{150}{90}$ $\frac{P}{R} = \frac{148}{50}$ 21-9-32. B.P. $\frac{142}{70}$ $\frac{P}{R} = \frac{102}{25}$ Systolic murmur loudest at pulm. area.	Gram-positive spore formers, morphologically similar to <i>B. subtilis</i> . Agglutination: Typhoid—1/160. Para A—nil. Para B—1/40. Eye: Vision—R. E. 6/8. L. E. 6/18. Tension both eyes 31 mm. Field—normal. Urine: acid albumin—a trace. Iron, strychnine, tr. ephedra, digifortis. Cured.
11	Jew, F., 13, œdema both legs, 1 month; whole body red; no diarrhoea; no fever; no palpitation; knee jerks exaggerated (left more than right). All along in Calcutta.	31-8-32. Jugular and suprasternal pulsation; apex in 5th and 6th interspaces, 3½ inches from midsternal line; systolic bruit maximum in pulm. area. B.P. $\frac{105}{70}$ $\frac{P}{R} = \frac{96}{22}$ 5-9-32. Right jugular—normal. Left jugular—slightly full and pulsating; suprasternal pulsation; systolic bruit maximum at pulm. area. B.P. $\frac{112}{65}$ $\frac{P}{R} = \frac{108}{24}$	Gram-positive bacilli. Urine: specific gravity—1010. Reaction—acid. Albumin } nil. Sugar } Iron, mag. sulph., tr. ephedra. Cured.
12	H., M., 58, œdema legs, followed by diarrhoea, dyspnoea, palpitation (after exertion) 3 weeks; fever 2 weeks; all other family members suffering from similar complaints. Eyes—cataract (?). All along at Barasat.	31-8-32. Orthopnoea, general anasarca ascites, hydrothorax; jugulars full, carotid and suprasternal pulsations; liver, lungs, engorged; apex in 6th interspace 5½ inches out; systolic bruit loudest at pulm. area and wholly replaces first sound; mitral leak. B.P. $\frac{116}{75}$ $\frac{P}{R} = \frac{112}{42}$ 2-9-32. Condition same. B.P. $\frac{130}{75}$ $\frac{P}{R} = \frac{120}{40}$	Gram-positive cocci. Gram-positive diplococci. Urine: Reaction—acid. Sp. gravity—1010. Albumin } nil. Sugar } Iron, strychnine, tr. ephedra. Left hospital on own responsibility.
13	H., F., 50, œdema legs, hands 2 months; breathlessness, palpitation 1 month; skin, legs and hands glossy; epigastric pulsation present; knee jerks normal; three family members suffering from similar complaints. All along at Barasat.	31-8-32. Orthopnoea, general anasarca ascites, hydrothorax; jugulars full, carotid and suprasternal pulsations; liver, lungs, engorged; apex in 6th interspace 5½ inches out; systolic bruit loudest at pulm. area and wholly replaces first sound; mitral leak. B.P. $\frac{116}{75}$ $\frac{P}{R} = \frac{112}{42}$ 2-9-32. Condition same. B.P. $\frac{130}{75}$ $\frac{P}{R} = \frac{120}{40}$	Gram-positive spore formers (not of <i>vulgatus</i> group). Gram-positive cocci. Urine: Reaction—acid. Sp. gravity—1010. Albumin—a trace. Sugar—nil. Iron, strychnine, paraldehyde medicinal, diuretic mixture, calcium lactate, digifortis, potass. bromide, tr. ephedra, strychnine, digitalin, brandy, glucose, leeches on cardiac region, cardiazol, oxygen. Died 10 days after admission.
14	H., M., 16, œdema legs, 1 month; palpitation, pain chest, debility 1 week; knee jerks exaggerated; sisters suffering from similar complaints; malaria off and on 2 months. All his life at Nalkorah (24-Pergannas).	Signs of advanced congestive failure similar to those described above.	Gram-positive organisms. Agglutination: Typhoid—1/160. Para A—nil. Para B—1/40. Shiga } nil. Flexner } W. R.—doubtful. Mist. salina. Left hospital on own responsibility.

Table of cases—contd.

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
15	H., M., 38, œdema legs, 1 month; pain thighs, palpitation, cough with expectoration later on, these were preceded by diarrhœa which lasted for 6 days; knee jerks exaggerated (right more than left); wife, son, niece suffering from similar complaints; Eye: dim vision—1 year; tension normal. All along at Dum-Dum.	Signs of advanced congestive failure similar to those mentioned above.	Scanty Gram-positive spore formers (no Gram-positive spore formers of the <i>vulgatus</i> group on culture). Urine: Reaction—acid. Sp. gravity—1020. Albumin } nil. Sugar } Midstream urine—sterile on culture. Sputum: Streptococci. Spirochætes. Yeast. Polymorph. cells. Lymphocytes. Iron, strychnine, expectorant mixture, tr. ephedra, calcium lactate, pandigal. Cured.
16	H., F., 40, œdema, legs, followed by palpitation, headache, occasional slight, fever 3 months; knee jerks exaggerated; five members in the family suffering from similar complaints; paratyphoid 7 months ago. All along in Calcutta.	Do.	Gram-positive spore formers; none on culture. Eye: R. E.—V with glass 6/9. T=23. L. E.—V with glass 6/9. T=40 (glaucoma left eye) Iron, strychnine. Cured.
17	H., F., 30, fever, diarrhœa 3 months; œdema legs 2 months; palpitation 3 weeks; legs are glossy; knee jerks normal; a few other members in the family suffering from similar complaints; malaria off and on; cholera 4 months ago. All along at Barasat.	Do.	Gram-positive spore formers (identical with <i>B. vulgatus</i> morphologically). Iron, strychnine, tr. ephedra, expectorant mixture. Left hospital on own responsibility.
18	I. Ch., F., 18, œdema, legs, 5 weeks; cough, palpitation 3 weeks; bowels 3 to 4 times a day but not loose; crepitations at right base; mother, brother suffered from epidemic dropsy lately; anæmia present. All along in Calcutta.	Do.	Gram-positive spore formers of the <i>vulgatus</i> group. Urine: Reaction—acid. Sp. gravity—1020. Albumin—a trace. Sugar—nil. Sodium sulphate, digifortis, medinal, strychnine, pandigal, calcium lactate, leeches over hepatic region, parathyroid, adrenalin, brandy, strophanthin. Died 5 days after admission.
19	H., M., 14, œdema, legs, fever, pain body 3 weeks; dyspnœa on slight exertion later on; palpitation 5 days; knee jerks exaggerated (right more than left); legs are glossy; parents suffering from similar complaints. All along at Dum-Dum.	Do.	Both Gram-positive and Gram-negative spore-bearing organisms; no Gram-positive spore formers on culture. Urine: Reaction—alkaline. Sp. gravity—1020. Albumin } nil. Sugar } Eye: L. E.: a patch of retinal hæmorrhage. No cupping of optic disc. R. E.: Fundus oculi healthy. Potass. bromide, digifortis, calcium lactate, brandy, pandigal, atebirin. Cured.

Table of cases—concl.

No.	Race, sex, age and history	Cardiovascular manifestations	REMARKS
20	H., M., 11, fever, œdema, legs, 3 months; palpitation 2½ months; anæmia present; grand-mother, cousin, sister suffered from epidemic dropsy but now cured. All along in Nadia.	Signs of advanced congestive failure similar to those mentioned above.	Gram-positive spore formers but none on culture, occult blood present. Iron, strychnine. Cured.
21	H., M., 27, fever followed by œdema legs, 1½ months; knee jerks normal; dysentery 8 years ago; kala-azar 6 years ago; 3 months in Calcutta. Previous residence Dacca.	Do.	Microfilaria. Urine: Reaction—acid. Sp. gravity—1010. Albumin } nil. Sugar } Treatment mainly dietetic. Cured.
22	H., F., 28, dysentery followed by œdema legs one month; rash, hæmorrhoids; lungs: right—crepitations at the base; left—a few occasional râles; knee jerks lost (?); fever off and on 2 months; a few other family members suffering from similar complaints.	Do.	Scanty Gram-positive spore formers. Agglutination against <i>B. vulgatus</i> (isolated from No. 6)—negative. Urine: Reaction—acid. Sp. gravity—1010. Albumin } nil. Sugar } B. T. Digifortis, liniment camph. co., brandy, tr. ephedra, medinal, atebirin.

Abbreviations used:

H., M. = Hindu male.
M., M. = Mohammedan male.
A. I. = Anglo-Indian.
H., F. = Hindu female.
M., F. = Mohammedan female.

Pulm. = pulmonary.
B. T. = benign tertian malaria.
B. P. = blood pressure.
P. = Pulse.
R. = Respiration.

R. E. = right eye.
L. E. = left eye.

CARBON TETRACHLORETHYLENE IN THE TREATMENT OF HOOKWORM INFECTION

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CARBON TETRACHLORETHYLENE was first suggested for the treatment of hookworm infection by Hall and Shillinger (1925). It was tried by several workers in different parts of the world and most of these investigators gave favourable reports on its use. We (Maplestone and Mukerji, 1929) tried it and did not find it very efficient, but we were only able to obtain it in soft gelatine capsules each of which contained half a c.cm. of the drug. We administered the tetrachlorethylene both in the capsules and removed from them, in some cases combining it with oil of chenopodium and in others giving it alone. The number of cures obtained by all of these methods considered together only worked out at 20.7 per cent, which was less than half of that obtained previously with carbon tetrachloride used in the same sized dose and in similar combinations. In addition to its

apparent ineffectiveness we found that just as many persons suffered from giddiness, nausea and vomiting after taking tetrachlorethylene as they did after tetrachloride, and as we have never seen any more severe symptoms than these after the use of the latter drug in Calcutta we expressed the opinion that the two drugs appeared to be equally toxic as far as we could judge from the symptoms produced, and Brosius, Peon and Carroll (1927) came to the same conclusions as ourselves. We accordingly discontinued the use of tetrachlorethylene until Lamson, Brown and Ward (1932) pointed out that such symptoms as the above are not evidence of dangerous toxicity, but are only those produced by any diffusible stimulant. On account of this statement we obtained a fresh supply of tetrachlorethylene, this time not in gelatine capsules, and submitted it to a further trial.

Before using it again in the treatment of patients, however, we decided to test it on cats. Our reason for doing this was that when carbon tetrachloride was first recommended for treatment of hookworm infection it was said by American workers to be safe for both dogs and cats, but when Chandler and Chopra (1925) tested this drug on Calcutta cats they found it

unaccountably toxic to these animals, so we thought it better to test tetrachlorethylene in the same manner before again using it on human beings. The result of our work on cats has been given recently in a paper by Maplestone and Chopra (1933), where it was shown that in very large doses the drug causes death of cats with some damage to the liver and kidneys; it can be given to these animals in thirty times the relative dose we have used for human beings without causing more than slight congestion of the liver and kidneys, and without any damage to the cells of either. We have also shown that alcohol does not increase its toxicity, and so we feel justified in stating that it is a much safer drug to use than is carbon tetrachloride, and unless it is given to patients suffering from severe intercurrent disease it is unlikely to produce dangerous symptoms, much less death.

Tetrachlorethylene does not appear to have come into general use as an anthelmintic, and in the last three or four years little has been written about it. The most important paper is one by Lambert (1933) in which he records over 46,000 treatments with this drug in the South Sea islands without a death and without any untoward symptoms, but he notes that it has a more exhilarating effect than tetrachloride, which as we have explained above is not to be taken as evidence of toxicity. Garin, Rousset and Gonthier (1931) describe using tetrachlorethylene in doses of three grammes, four grammes and five grammes respectively on three consecutive days giving the drug in doses of one gramme at hourly intervals. They kept their patients in bed or confined them to their rooms during the treatment, so their method is not of any use for employment in the treatment of labour forces, but as the only symptoms complained of by their patients were drunkenness and giddiness immediately after taking the drug, their report indicates that tetrachlorethylene cannot be very toxic. Kendrick (1929) reported on about fifteen hundred treatments with tetrachlorethylene in doses of three c.cm., and in this series he had one man who exhibited severe symptoms. This patient appeared healthy but he soon became unconscious after receiving the drug, he remained in this state for about three hours, and he was so collapsed that it was thought necessary to give him an injection of strychnine and digitalin. After recovering consciousness this man rapidly improved and two hours later was apparently normal. Ten other persons were treated at the same time as this man with the same sized dose of the drug and none of them showed any signs of toxicity. The above is the only case of dangerous toxicity yet recorded from the use of tetrachlorethylene as far as we know, and so far there have been no deaths.

This isolated experience of Kendrick's suggests the possibility that a few persons exist who have an idiosyncrasy to tetrachlorethylene, just as there appear to be in the case of tetrachloride,

but the similarity between the two drugs ends here for tetrachloride always damages the liver and frequently the kidneys, whereas tetrachlorethylene does not have any damaging effect on these organs.

Method of administration.—In our previous work on this drug we found that it was similar to tetrachloride in that it was just as effective when given with the purgative as when the giving of the purgative was delayed for one or two hours. Accordingly we have followed the same routine in the use of this drug as we have previously employed in giving tetrachloride. For a considerable time before we began to use tetrachlorethylene we used tetrachloride and oil of chenopodium in combination in all our hookworm cases. Our reason for using the two drugs is that the cure rate is slightly higher than when tetrachloride is given alone, and as the majority of patients have an ascaris infection as well the oil of chenopodium acts on these worms too. The maximum dose of oil of chenopodium we employed in combination with tetrachloride is one c.cm., which is well within the safety limit of toxicity of this drug, and in the present series of cases treated with tetrachlorethylene we have used the same amount of oil of chenopodium as well.

The actual details of treatment are the following, which we have now used for some years in the case of tetrachloride without any ill-effects. It will be seen that it has the advantage of being both simple and cheap in that it does away with the use of gelatin capsules.

Two ounces of saturated magnesium sulphate solution are placed in a flask or bottle of three or four ounces capacity and four c.cm. of tetrachlorethylene and one c.cm. of oil of chenopodium are added to it. The flask is corked and shaken until the drugs are distributed throughout the mixture in the finest possible droplets; the dose is then given to the patient immediately, before the drugs have time to coalesce into larger drops and float to the surface, as they will do if the mixture is left standing. This method of shaking was adopted in the first place because it was stated that it was dangerous to give tetrachloride unless it was in finely divided droplets, and the same method has been continued with tetrachlorethylene because we consider that the even diffusion of the drug throughout the draught gives it a much better chance of coming into contact with all the worms on the gut wall and it is therefore more efficient than if given as an undivided globule of one drachm.

Although the work of Garin et al. quoted above indicates that tetrachlorethylene can be repeated with safety for two or three days in succession we do not recommend its being given under less than ten-day intervals, because it resembles other anthelmintics in causing the female hookworms to stop egg-laying for some days when it fails to remove them, and so the

establishment of a cure cannot be determined under that time.

Results of treatment.—We have treated fifty cases under hospital conditions and we have cured thirty-one (sixty-two per cent) with the first treatment and a further six (twelve per cent) with two treatments. The cure rate after the second treatment would probably have been higher but ten of the remaining thirteen persons left hospital before it could be given to them, thus there were only four patients out of the fifty that we definitely know were not cured by two treatments. Our standard of cure has been a negative result with Lane's centrifuge at least ten days after treatment, we have not made egg counts to estimate the percentage reduction of worms because as we have formerly pointed out (Maplestone and Mukerji, 1932) we consider deductions made from these counts unreliable.

Twenty-one of our patients felt slight giddiness, nine vomited, four felt nausea but did not vomit, and one said he felt drowsy for a short time. Of the nine persons who vomited two did so immediately and the others at periods ranging between one and three hours after swallowing the dose; the dose was not repeated so the vomiting probably had some effect on the total cure rate, and this supposition is supported by the fact that only two of the nine who vomited were cured by one treatment. This record of intoxication appears somewhat formidable at the first glance for the total number exhibiting symptoms appears to be thirty-five, but the actual number of individuals so affected was thirty as some of them showed more than one of the symptoms mentioned. Also it should be noted that the symptoms were never severe, and as we were dealing for the most part with uneducated persons the presence or absence of these symptoms had to be elicited by leading questions so it is possible that suggestion played a considerable part in deciding the nature of the replies given. Both Kendrick and Lambert, quoted above, also found that tetrachlorethylene is more exhilarating than tetrachloride, but with the exception of the one case of Kendrick's none of these symptoms were severe and only resembled those of alcoholic intoxication. Lambert says he has often observed coolies deliberately exaggerating the effects of tetrachlorethylene for the amusement they seemed to derive from appearing more drunk than their fellows. This is an important thing to remember when using the drug on a large scale with numbers of coolies being treated at once and looking on at the treatment of others.

After the work recorded in this paper was finished we noticed a paper by Christensen and Lynch (1933) in which, as a result of experiments on dogs, they state that tetrachlorethylene in therapeutic doses causes considerable depression of the heart and respiration, but they give no details as to the amount of the depres-

sion produced nor how it was estimated. On account of this statement we have tested these effects on ten patients. Our method of doing this was to take the pulse and respiration rates and the blood pressure immediately before giving the usual dose of tetrachlorethylene and oil of chenopodium, and to repeat these readings one hour and two hours afterwards. Our results are shown in the table.

TABLE
Effect of tetrachlorethylene on the respiration and circulation

Case number		TIME READINGS WERE TAKEN		
		Before dose	1 hour later	2 hours later
1	Pulse per min...	92	92	88
	Resp. per min...	18	22	24
	Blood pressure ..	120/65	110/60	114/54
2	Pulse per min...	72	76	80
	Resp. per min...	20	18	20
	Blood pressure ..	110/70	100/60	102/64
3	Pulse per min...	60	64	60
	Resp. per min...	20	20	20
	Blood pressure ..	100/60	105/60	100/65
4	Pulse per min...	68	68	60
	Resp. per min...	24	20	24
	Blood pressure ..	110/70	100/55	95/55
5	Pulse per min...	80	88	84
	Resp. per min...	20	16	20
	Blood pressure ..	120/95	114/90	114/85
6	Pulse per min...	68	64	68
	Resp. per min...	20	20	20
	Blood pressure ..	120/50	118/50	112/48
7	Pulse per min...	64	64	60
	Resp. per min...	20	20	24
	Blood pressure ..	120/70	114/68	104/60
8	Pulse per min...	88	80	76
	Resp. per min...	20	16	20
	Blood pressure ..	100/54	94/54	90/58
9	Pulse per min...	76	80	80
	Resp. per min...	24	20	20
	Blood pressure ..	100/62	94/64	96/64
10	Pulse per min...	80	68	60
	Resp. per min...	16	16	20
	Blood pressure ..	120/78	120/74	118/70

It will be seen from these figures that there is no constant or significant change in the pulse and respiration rates, and although there appears to be a definite tendency for the blood pressure to fall in all the cases this is so slight as to be negligible in practically every instance. With regard to changes in blood pressure it should be borne in mind that blood pressure is a constantly varying quantity and that it may be considerably influenced even by mild excitement. The patients we examined in this way were all

Indians of a low standard of education so that it is possible that the appearance of the sphygmomanometer and the manipulations attendant on taking the readings may have somewhat excited them and caused a slight rise of blood pressure on the occasion of taking the first reading when they did not know what was going to happen next, but as this element of uncertainty was absent on the two subsequent readings the blood pressure remained unaffected. In any case, whether the circulatory changes observed by us after administration of tetrachlorethylene were real or apparent, they are so slight according to the evidence obtainable by clinical examination that we are unable to agree with Christensen and Lynch when they say that it causes considerable depression.

These workers also say that tetrachlorethylene caused damage to the small intestine both in single and repeated doses, but we saw no macroscopic evidence of this in our work on cats so did not examine this organ microscopically. We have already published our results regarding the damage done to the liver and kidneys of cats (Maplestone and Chopra, 1933) and as far as our work went we cannot agree that this drug causes any appreciable damage to these organs when given in single doses much in excess of the therapeutic amount, and we are much more inclined to agree with Lamson, Robbins and Ward (1928) who consider tetrachlorethylene is safe in respect of the liver and kidneys. Christensen and Lynch also claim that considerable damage is done to the heart tissue by tetrachlorethylene. We have not yet made any experimental observations on the effect of this drug on the heart so we are unable to comment on their statement except to say that there is no clinical evidence of damage of this nature.

Our cure rate with tetrachlorethylene is slightly greater than it was with tetrachloride, but we gave one c.c.m. more of the former drug than we did of the latter, and this may explain the difference, but even if this is the explanation of the higher number of cures with tetrachlorethylene the practical advantage of it still remains, because if it can be safely given in larger doses than tetrachloride and cures more persons it is therefore a better drug for the purpose of curing hookworm infection. The price of tetrachlorethylene is slightly higher than that of tetrachloride at present, but that is of little importance because from the price quoted by one firm of manufacturing chemists we find that a dose of four c.c.m., or one drachm, will only cost half an anna.

Conclusion

Tetrachlorethylene, used after the method described above, is at least as efficient as tetrachloride, and it is safer than the latter on

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FEVERS IN PREGNANCY

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IN our experience at the Eden Hospital, *Bacterium coli commune* infection of the urinary tract has been found the commonest cause of fever in women during the period of gestation. Seventy-two pregnant patients were admitted into the Eden Hospital with fever in the year 1932, and of these 57 (79 per cent) had *B. coli* infection of the urinary tract.

Why should *B. coli* infection be so common with pregnancy? Various explanations have been offered, and it is generally agreed that the infection is blood-borne. Horder is of the opinion that constipation, which is very common during pregnancy, is responsible for minute ulcerations ('fretting' is the term used) in the mucous membrane of the large intestine. Through these ulcerated areas *B. coli* gain access to the blood and lymph streams. They are

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account of its not damaging the liver and kidneys when given in therapeutic doses. Another great advantage, especially when dealing with a large labour force, is the fact that alcohol does not increase its toxicity.

REFERENCES

- Brosius, O. T., Peon, I. E., and Carroll, R. L. (1927). Tetrachlorethylene in Uncinariasis, a preliminary report. *United Fruit Company Med. Dept. 16th Ann. Rep.*, p. 183.
- Chandler, A. C., and Chopra, R. N. (1925). The Toxicity of Carbon Tetrachloride to Cats, a Warning. *Indian Med. Gaz.*, Vol. LX, p. 406.
- Christensen, B. V., and Lynch, H. J. (1933). The Effect of Anthelmintics on the Host. I. Tetrachlorethylene. II. Hexylresorcinol. *Journ. Pharm. and Exper. Therap.*, Vol. XLVIII, p. 311.
- Garin, N. C., Rousset, J., and Gonthier, B. (1931). Tetrachlorethylene a New Anthelmintic. *Bull. Mém. Soc. Méd. Hôpit. de Paris*, Year 47. (Rev. Trop. Dis. Bull., Vol. XXIX, p. 39.)
- Hall, M. C., and Shillinger, J. E. (1925). Tetrachlorethylene a New Anthelmintic. *Amer. Journ. Trop. Med.*, Vol. V, p. 229.
- Kendrick, J. F. (1929). The Treatment of Hookworm Disease with Tetrachlorethylene. *Amer. Journ. Trop. Med.*, Vol. IX, p. 483.
- Lambert, S. M. (1933). Hookworm Disease in the South Pacific. Ten Years of Tetrachlorides. *Journ. Amer. Med. Assoc.*, Vol. C, p. 247.
- Lamson, P. D., Brown, H. W., and Ward, C. B. (1932). Anthelmintics. Some Therapeutic and Practical Considerations on Their Use. *Journ. Amer. Med. Assoc.*, Vol. XCIX, p. 292.
- Lamson, P. D., Robbins, B. H., and Ward, C. B. (1928). The Pharmacology and Toxicology of Tetrachlorethylene. *Amer. Journ. Hyg.*, Vol. IX, p. 430.
- Maplestone, P. A., and Chopra, R. N. (1933). The Toxicity of Tetrachlorethylene to Cats. *Indian Med. Gaz.*, Vol. LXVIII, p. 554.
- Maplestone, P. A., and Mukerji, A. K. (1929). Tetrachlorethylene in the Treatment of Hookworm Disease. *Indian Med. Gaz.*, Vol. LXIV, p. 424.
- Maplestone, P. A., and Mukerji, A. K. (1932). Hexylresorcinol as an Anthelmintic. *Indian Med. Gaz.*, Vol. LXVII, p. 610.

forthwith excreted through the kidneys if functioning normally, but usually there is a mechanical obstruction to the flow of the urine from the pelvis of the kidney to the bladder during the first few months of pregnancy. The rising uterus tends to press on the ureter, at the brim of the pelvis. The uterus reaches there at the fifth month and symptoms appear in the majority of the cases from that month onwards. The pressure, no matter how slight, is enough to obstruct the free flow of urine and the pelvis of the kidney or kidneys dilates slightly and there is an incipient hydro-ureter and a consequent hydronephrosis. The retained urine harbours the *B. coli* excreted from the blood and a mild pyelitis results, manifesting itself by fever, dysuria and pain in the back. The pain is usually unilateral and is commoner on the right than on the left side; this is due perhaps to the normal dextro-deviation of the uterus. Superficially this explanation seems convincing but obviously it is not final, because we have not been able to grow *B. coli* from the blood stream of all patients suffering from pyelitis during pregnancy. We have tried to prove the mechanical part of the theory in the following manner. In an intelligent primipara who was admitted with fever in the eighth month of pregnancy, the presentation was changed from a vertex to a breech and the uterus was pushed to beyond the middle line on the left side and kept there with pads, and an abdominal binder was applied. The nurse was instructed to make the patient lie on the left side and not to allow her to lie on her back. Twelve hours afterwards the patient said that her pain was gone, and the dysuria was much less but there was no difference in the temperature. Encouraged by this experiment, a routine podalic version and a forced sinistro-deviation of the uterus has been done on six cases, with appreciable relief of pain but without any remarkable difference in the excursions of the temperature.

An Armenian patient, a primipara, was admitted into the hospital thrice between her fifth and ninth months, each time with high fever. A pure growth of *B. coli* was obtained every time from the urine. On the last occasion this patient died in a condition of coma two hours after admission. A post-mortem Caesarean section was done to recover a living child if possible, and the opportunity was availed of to inspect the kidneys. Both the pelves were distended and the ureters, when exposed, were found to be dilated.

It is far from easy to treat these cases of pregnancy pyelitis. Like benign tertian malaria a single attack can usually be controlled, but it is a very obstinate infection to eradicate completely. The first step in the treatment is to empty the bowels with a suitable purge by mouth, followed in two or three hours time with a bowel wash of normal saline containing two grains of potassium permanganate to the pint.

The next step is to administer alkalis in massive doses till the urine is completely alkaline. Our practice is to prescribe citrate of potassium in drachm doses repeated three or four times in the day because bicarbonate of soda is not tolerated by these patients. It has been found that a good way of giving the potassium salt is in combination with a tablespoonful of glucose 'D' (Sandoz) or sugar-of-milk dissolved in a wine-glass of water. After intensive alkaline treatment acids are exhibited, acid sodium phosphate in ten-grain doses is administered followed by a ten-grain cachet of hexamine twice or three times a day. Acids are not tolerated by some patients and they complain of either frequency of micturition or actual burning during the act. If this occurs the treatment is immediately discontinued and the bladder may have to be washed out with normal saline and it is advantageous to put one ounce of a one per cent solution of mercurochrome into the bladder. When there is actual cystitis a self-retaining catheter is introduced into the bladder and kept there for a couple of days. Oral administration of hexamine is not always so effective as it is by the intravenous route. In all protracted cases of fever of *B. coli* origin a course of intravenous injections of 5 c.cm. of a 40 per cent solution of urotropin is very useful. Once the temperature is well controlled or moderated to excursions of a degree or a degree and a half per day, Horder recommends salol and hydrargyrum cum creta in five-grain doses by the mouth twice daily for four days in the week.

Vaccines have not been found very efficacious in the treatment of the *B. coli* infection during pregnancy. Pathologists explain this failure by the fact that they do not always get a pure growth from the culture of the urine. Stock vaccines or autovaccines prepared from a culture of the urine have not proved of any use in the limited number of cases in which we used them. Mr. Wade of Edinburgh irrigates the pelvis of the kidney with normal saline solution in obstinate cases. We have not had the opportunity of trying this method of treatment. Passing a ureteral catheter is useful in that it dilates the strictures in the ureters and makes it possible for the urine to flow more freely.

Malaria and kala-azar are not such frequent complications of pregnancy as might be expected from the prevalence of these diseases in this part of the world. In fact primary malarial infection during pregnancy in an Indian is a rare event. In a series of 21 cases of primary malarial infections during pregnancy, 4 were Europeans, 1 was an American, 1 a Japanese, 3 were Chinese, 8 were Anglo-Indians and the remaining 4 were Indians whose previous history of having fever was indefinite. The American, the Japanese, and two of the three Chinese patients had come to this country within three months of being infected and, of the nine

foreigners, in seven the infection was that of a malignant tertian fever. In our limited experience at the Eden Hospital and at a maternity and child welfare clinic run by a missionary society in Calcutta, the incidence of kala-azar during pregnancy is infrequent. In one year in a series of 1,940 cases, the sera of only 17 patients running a temperature were returned as positive to the aldehyde and urea stibamine tests. In addition to these, in 32 cases where the clinical picture was one of kala-azar, urea stibamine was tried empirically with very good results. In our hands quinine has not yet interrupted the course of pregnancy in patients where the malarial parasite has been found in the blood and where the patient has been given alkalis along with the quinine. We never use quinine intravenously but only by the oral or intramuscular route. We tried atabrin in three cases of benign tertian infection with encouraging results and we did not meet with any discoloration of the skin. We have not used plasmochin.

Intestinal parasites are very often responsible for the febrile condition during pregnancy. Gurkha women and people from the Northern parts of the adjoining areas of Bihar and the United Provinces suffer from heavy helminthic infections.

Intra-uterine death of the foetus occasionally is the cause of a rise in the temperature. In the early months of gestation the ovum may separate from the wall of the uterus, totally or partially. If it is not expelled it remains in the uterus as a carneous mole. The rise in the temperature may be due to the absorption of fibrin from the intra-uterine extravasated blood. In the later months when interruption in gestation occurs, disintegration of the foetus, the placenta and the membranes takes place and absorption of these products possibly reacts on the mother, producing 'fever'. Beyond the rise in temperature and a feeling of malaise there may not be any definite indication pointing to the death of the foetus. If the symptoms are not urgent, it is safe to wait for a fortnight, or if possible for a month and, at the end of the period, examine the uterus to find out if it has enlarged in size. If the uterus remains stationary or retrogresses, suspicion as to the death of the foetus is confirmed. In more advanced pregnancies absence of foetal heart sounds and foetal movements, where there were such sounds and movements previously, clinches the diagnosis at once. X-rays help the diagnosis in advanced cases. A flattened and deformed calvarium, a hyperflexed or super-extended spine, and irregularly placed limb bones all point to the fact that the foetus is dead and the skeleton is in the process of intra-uterine maceration. It is easy to empty the uterus of the products of conception in the later months, but in the early months it is not always

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TOXIC EFFECTS OF EPHEDRINE—A WARNING

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and

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THE alkaloid ephedrine is obtained from several species of ephedra growing in China and India. Under the name of *Ma Huang* this herb has been in use in the Chinese indigenous medicine for about 5,000 years. The development of a useful modern drug out of this ancient remedy is due to the pioneer work of a Japanese chemist, Nagai (1887), who isolated this alkaloid in a pure form and two Japanese physiologists, Amatsu and Kubota (1917), who demonstrated the essentially sympathomimetic (epinephrine-like) effects produced by ephedrine. Chen and Schmidt (1924) reopened the therapeutic possibilities of the drug by conducting a series of careful studies with regard to its physiological properties. Chopra and his collaborators (1929, 1930, 1931) did a large amount of work on the Indian species of ephedra and worked out many points in connection with the pharmacological action and therapeutic properties of not only ephedrine but the allied alkaloid, pseudo-ephedrine.

The result of all this work has been that during the last ten years ephedrine has risen from obscurity to a widespread popularity among medical men in all parts of the world.

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so easy. The placenta is in most cases adherent and does not separate easily. We use and recommend the very safe and simple technique of introducing laminaria tents into the uterus along with the injection of glycerine and tincture of iodine into the uterine cavity. This operation is carried out as follows:—The patient is in the lithotomy position; no anaesthetic need be used. Two or three laminaria tents are introduced into the uterine cavity the first day, and after twenty-four hours these are removed, a thick india-rubber catheter (no. 12 Jacques) is introduced into the uterine cavity through which pure sterile glycerine and tincture of iodine (seven drachms of glycerine and one drachm of iodine) is injected into the uterus. At the same sitting three or more fresh tents are introduced. The uterus usually empties itself completely after this but occasionally four half-hourly injections of 0.25 c.cm. of pituitrin may be necessary.

The above observations have been made under the guidance of Lieut.-Colonel V. B. Green-Armytage, M.D., F.R.C.P., F.C.O.G., to whom I am grateful for allowing me to use the records of the Eden Hospital and to publish records of some of his patients.

Its range of utility is so wide that there is hardly a medical practitioner who has not had occasion to use the drug some time or other in the course of his professional career. The therapeutic claims made for the drug were examined by the Council of Pharmacy and Chemistry of the American Medical Association in 1926 and they were so struck by the potency and usefulness of the alkaloid that it was at once introduced into the United States Pharmacopœia. The new sixth edition of the British Pharmacopœia published in 1932 has also recognized it and it has now become an established remedy.

At the present time this alkaloid is widely used for a variety of conditions and the literature is full of many interesting and instructive articles regarding its pharmacological action and therapeutic uses. It has been used with success in the treatment of bronchial asthma, hay fever, whooping cough, bronchitis, postural hypotension and Stokes-Adam's syndrome. It has been employed in combating the fall of blood pressure in spinal anæsthesia, in antagonizing the action of narcotic drugs, in shrinking the congested nasal mucous membrane, and in dilating the pupil for ophthalmic examinations. Its effects in allergic dermatitis, shock and dysmenorrhœa are promising. Of all the diseases for which the drug has been tried, asthma is the commonest condition. The fact that it can be effectively given by the mouth and that its action is more lasting than epinephrine has made it a very popular remedy. Its reputation as an efficient anti-asthmatic has spread even amongst laymen and in many cases the drug is taken on a patient's own initiative without his consulting a physician.

From time to time attention has been called to certain untoward effects from the use of this drug whether given by the mouth or by injection. Miller (1925) by using doses of 50 to 125 mgm. (0.75 to 1.87 grains) found no definitely harmful effects but recorded that a few patients complained of palpitation, nervousness and nausea. One who had marked myocardial degeneration showed a transient pulsus alternans one hour after the drug was administered. Production of nausea after administration of the drug in cases of asthma and hay fever was reported by Althausen and Sehmacher (1927). Anderson and Homan (1927) used ephedrine in whooping cough in children. Though the drug was efficacious in preventing the spasmodic attacks, they observed in several cases marked restlessness, sweating, abdominal pain, discomfort, and apparent suppression of urine. That these symptoms were produced by ephedrine is shown by the fact that they disappeared when the drug was discontinued and reappeared when it was resumed. Middleton and Chen (1927) in a series of 41 patients found that palpitation of the heart was the prominent feature when the dose of ephedrine was larger

than 80 mgm. (1½ grains); vomiting, dizziness, nervousness, headache and insomnia were also observed in several cases. Tremors, weakness, sweating, and sometimes a feeling of warmth all over the body were also noted. These symptoms usually abated shortly after the blood pressure began to fall; this fall occurs in one to seven hours after administration. Four out of eleven cases in this series showed extrasystoles of ventricular and auricular origin after ephedrine which could be demonstrated with the electro-cardiograph. Another patient developed paroxysms of tachycardia which lasted for a few minutes at a time and then stopped. Bloedorn and Dickens (1928) described a case of cardiac asthma in which cardiac embarrassment, including pulsus alternans, marked tachycardia and cardiac decompensation occurred after administration of ephedrine. Pennetti (1928) observed, by means of electrocardiography, that ephedrine increased the frequency of pre-existing extrasystoles in two cases but produced no change in a case of auriculo-ventricular block of vagal origin. Chopra and his co-workers (1929) first pointed out in this country the dangers which may attend the indiscriminate use of this alkaloid. During recent years a number of cases have come to our notice which leave little room for doubt that the serious effects of the alkaloid have not been fully appreciated by the medical profession in this country. An analysis of the history sheets of a large number of patients in our asthma clinic revealed the frequency with which certain unpleasant side-effects were produced following the administration of ephedrine. We have therefore thought it necessary to give the results of our experience and sound a note of warning regarding its indiscriminate use.

TOXIC EFFECTS

Acute onset.—The most usually noted unfavourable symptoms in our series have been those referable to the *cardiovascular system*. Acute precordial pain resembling an attack of angina with palpitation and profuse sweating, particularly on the forehead, has been found quite commonly. In many persons these symptoms are not acute enough to be particularly noticed or to call for any immediate attention or interference. Tremors of the extremities; a feeling of warmth, flushing all over the body and a dull throbbing sensation in the region of the temples have not uncommonly been complained of by the patients. Faintness; loss of muscular tone and disinclination to physical exertion were observed in two patients. Other symptoms were irregular and rapid pulse, widely dilated pupils, feeble heart beats, and dyspnoic type of respiration. In fair patients, a distinct flush in the malar regions and over the ears may be noticeable.

Disagreeable symptoms in connection with the *gastro-intestinal tract* are less commonly met

with. Nausea, vomiting and colic have been complained of by at least four individuals in our series. Both vomiting and nausea become more intense if the drug is given after a heavy meal. Nausea is sometimes intractable and continues for 24 to 36 hours, but generally disappears within 8 to 10 hours after the drug is stopped. Abdominal distress and a peculiar vague feeling of discomfort round the umbilicus were complained of by two patients. Loss of appetite is not infrequently produced. Constipation with associated flatulence and distension has been a common complaint in those taking the drug for prolonged periods.

Affections of the *genito-urinary system* are observed in the form of dysuria, anuria, and spermatorrhœa. One patient reported complete retention of urine for 24 hours after the administration of ephedrine (4 tablets in the course of 24 hours). No reliance was placed on his version but the presence of a fully distended bladder left no room for doubt. Application of heat and a gentle pressure from above helped him to pass large quantities of pale yellow urine easily. No reason for the retention of urine other than the use of ephedrine could be found in this case, and our opinion was corroborated by the fact that the condition recurred three days later when the drug was again taken and again disappeared when it was discontinued. Dysuria has been the prominent symptom in several patients. In one of these, albumin could be detected on examination of urine. There may be complete relaxation of the bladder sphincter resulting in involuntary micturition in some cases. Spermatorrhœa was complained of by two patients; one of them, a chronic asthmatic aged 46 years, refused to take the drug as it always induced a watery discharge from his urethra. Curiously enough, increase of sexual power has been reported by another who came back for the drug more for the aphrodisiac effects which he experienced than for the relief of asthma.

Many of the untoward effects referred to above have been noticed to occur in groups in the same individual. Thus, patients showing circulatory reactions usually complained of precordial pain, sweating, palpitation, flushing and tingling sensations simultaneously; very seldom has a single symptom been complained of. The effects become apparent within half an hour after administration of a dose and in the majority of individuals they pass away within 2 to 7 hours. Plethoric patients with systolic pressures above 120 to 130 mm. Hg. are more prone to get these side-effects.

In our series of patients we found that the toxic symptoms usually appeared in those who were having large and frequent doses of the drug. Doses below two grains daily rarely produced any symptoms except in sensitive individuals. No definite statement however can be made with regard to the relationship between

the dose and the appearance of the side-effects. The same dose may produce desirable and remarkably good effects in one patient but may produce equally beneficial results with some discomfort in another and may usher in a train of most undesirable symptoms in a third. According to Pollak and Robitschek (1926) and Gaarde and Maytum (1927) the development of these uncommon signs and symptoms does not depend so much upon the dosage but upon the stability of the nervous system of the individual taking the drug. We have at least two cases in our series in which we can definitely associate the appearance of these symptoms with a neurotic or a neuropathic tendency. Severe headache, faintness and a feeling of numbness in the extremities followed within twelve to fifteen minutes of administration of a half-grain tablet of ephedrine sulphate in one of these patients. Such cases fortunately are rare.

Ephedrine is considered to be a sovereign remedy against asthma and it is used more indiscriminately in this than in any other condition. Many of these cases are not true bronchial asthma and it is not unusual to find cases with involvement of the cardiovascular system being treated with ephedrine. If some of the toxic manifestations referred to above occur in cardiac cases, results may be dangerous. The following two cases are given by way of illustration:—

Case 1.—An Anglo-Indian working girl, aged 24, presented herself at the out-patient department of the School of Tropical Medicine, Calcutta, complaining of shortness of breath, cough, palpitation and a sinking feeling in the chest. She was diagnosed as a case of asthma by a private practitioner and was recommended an antispasmodic mixture and ephedrine hydrochloride tablets (gr. i each) at bed time or with the onset of an attack. The first night after only one tablet the patient felt fairly comfortable and slept well without any cough or paroxysm. The next day she had a busy day in the office and had to exert herself a little more than usual. That night there was a feeling of oppression in the chest, and palpitation and cough returned with increased intensity. She took three tablets of ephedrine one after the other. Within fifteen minutes she felt a sensation of giddiness and a sinking feeling; the precordial pain became intense and she felt that she was going to die. She was put to bed immediately, an ice bag was applied to the head and medical aid was sought. The patient however felt better by the time the doctor arrived but the pain in the chest remained in spite of the stimulants that were administered. Next morning as the asthmatic paroxysm persisted the patient took two more tablets without consulting the doctor, and the symptoms recurred with greater intensity. On examination she was found pale and cyanotic with dark rings round her eyes. She was using the accessory respiratory muscles when she talked and there was an anxious expression in her face. The tonsils were enlarged and slightly congested; râles were heard at the bases of both the lungs. The heart was definitely dilated with a rapid weak beat and a systolic bruit was audible at the mitral area. Systolic blood pressure was 120 mm. Hg., and diastolic 110 mm. Hg. Albumin and hyaline casts were found in the urine.

She gave a history of having rheumatic fever six years ago and another attack two years back. A diagnosis of asthma probably of cardiac origin was made and the patient was admitted into the Carmichael Hospital for

Tropical Diseases. In the hospital she was more thoroughly examined and the symptoms definitely attributed to heart failure. There was nothing to show that she was suffering from bronchial asthma. Ephedrine was tried in small doses and was found to aggravate the symptoms of cardiac failure and produced the symptoms above described. She was put on absolute rest in bed and digitalis, and the symptoms disappeared in the course of a fortnight.

Case 2.—A Hindu lady, aged 50, had been suffering from asthma for the last six years. She was treated outside with antispasmodics, vaccines, soamin, adrenalin, nasal cauterization, etc., without relief. She has taken ephedrine times without number for relief of paroxysms and always keeps a bottle by her for use in case of emergency. During the last attack for which she came under observation, she gave a history of having taken four ephedrine tablets within 1½ hours. Immediately there was a sensation of discomfort, precordial pain and distress which became unbearable. There was a hot flush all over the body and the abdomen was distended; flatulence, nausea and palpitation were very distressing. The patient also had intense headache and pain in the eyeballs.

Physical examination revealed a definitely dilated heart and thickened arteries, the chest was emphysematous (barrel-shaped) with sunken lower intercostals. The pulse rate was 100 per minute and there was evidence of missing beats. The blood pressure was rather high (155 mm. Hg. systolic and 130 mm. of Hg. diastolic) indicating hypertension. Albumin and granular casts were detected in the urine.

Ephedrine was discontinued and there was no recurrence of the symptoms. The patient was put to bed and kept under alkalies and digifortis and made a good recovery.

Chronic poisoning.—Prolonged use of ephedrine in therapeutic doses does not usually produce cumulative toxic effects. Individuals who suffer from paroxysms of asthma every night are enabled to remain free from attacks for long periods by taking this alkaloid in doses up to one grain once, twice or even three times every 24 hours. They can attend to their daily work and pass comfortable nights without any permanent ill-effects on the system. Experimental results also appear to bear out these observations. Middleton and Chen (1927) reported a case that received a total quantity of ten grains of ephedrine sulphate in a period of eleven days but showed no untoward effects. Wu and Read (1927) mentioned a case in which ephedrine therapy was continued for three years and caused no ill-effects. Chronic ephedrine poisoning however occurs though it is a much rarer condition. A pale, sallow and cyanosed appearance associated with a mild degree of anaemia has been frequently noticed in individuals who are in the habit of taking ephedrine for prolonged periods. Whether this is due to any toxic action of the drug or a natural sequence of the disease itself cannot be definitely stated without a thorough investigation on this point being made.

Habit formation is another undesirable result though it is debatable whether this ever occurs. It is common knowledge that gradually increasing doses are required by patients with chronic asthma for the relief of their attacks. This indicates increased tolerance if not actual habit

formation. In several of our patients we have noticed a peculiar sensation of euphoria produced by the drug. Withdrawal in those cases gives rise to a very uncomfortable feeling and the patients urgently demand to be allowed to resume the drug. Extreme nervousness and insomnia are also frequently met with. There was definitely some craving, though it was certainly not so intense as that felt after narcotic drugs. Whether this craving for the drug is a danger-signal of the early manifestation of a drug habit, or is due to the eagerness of the patients to ward off an impending attack it is very difficult to say. This observation is not in accord with that of Middleton and Chen (1927) and Thomas (1926) who believe that ephedrine is not a habit-forming drug. Higgins (1929) reported a case of chronic ephedrine poisoning which simulated hyperthyroidism in all its essential features, but we have not come across any case similar to the one described by him.

Discussion and comments

There is ample evidence to show both from a study of our own cases and from those recorded by other investigators that toxic manifestations and undesirable side-effects are not uncommonly met with after the use of ephedrine in asthma and other conditions. Some of the subjective symptoms are easily explained when one considers the physiological action the alkaloid produces on the system. Ephedrine in doses of 1 to 10 mgm. per kilogramme is known to cause a rise in blood pressure of anaesthetized dogs by 100 or more millimetres of mercury and it is maintained at this level for at least 15 to 25 minutes. In human beings, the rise in pressure is not so high as in animals but it varies from 20 to 65 mm. Hg. It is therefore easy to see that circulatory reactions like palpitation and anginal pain will be produced by the drug, particularly when the systolic pressure is at its highest level. The symptoms are also found to disappear as the pressure returns to normal. Insomnia and tremors are possibly due to stimulation of the central nervous system. Constipation, nausea and anorexia may be explained by the paralytic condition of the gut due to sympathetic stimulation and loss of tone. Headache and throbbing sensations in the temples may be attributed to changes in pressure in the arterioles or veins within the skull.

There is no agreement regarding the dosage required to produce these effects. Ephedrine is undoubtedly not a very toxic alkaloid and consequently there is a wide margin of safety. Its minimum lethal dose when given intravenously in dogs was found by Chen to be from 70 to 75 mgm. per kilogramme body weight. From this it can be inferred that a man weighing 50 to 60 kilogrammes would require about 4 to 5 grammes of the alkaloid to produce a fatal result. In contrast to this the usual therapeutic dose is from $\frac{1}{2}$ to 2 grains (65 to 130 mgms.)

and 7 grains (0.43 gramme) have been given in a single dose without untoward effects. The only explanation of the toxic effects appears to be a state of hypersensitiveness of certain individuals to the drug. Ephedrine is a sympathomimetic drug and stimulation of the sympathetic system in a highly-strung individual may lead to symptoms of sympatho-parasympathetic imbalance. It is also well known that slight differences in the amount of calcium in the blood make the autonomic system very sensitive to sympathomimetic drugs of which ephedrine is one.

Cautions and contra-indications

It should not be forgotten that ephedrine administration sometimes gives rise to unpleasant and dangerous side-effects. The commonest effects are attributable to its stimulant action on the circulation. All cases of asthma should therefore be thoroughly examined with regard to their heart condition before the drug is administered. Great caution should be exercised in using the drug in cardiac disorders especially when there are signs of failing compensation. In angina pectoris the drug is very dangerous. In chronic asthmatics with emphysema and arterial hypertension, ephedrine should not be prescribed.

Individual sensitiveness plays a great part in the production of the unfavourable symptoms. A small dose for one individual may be a large one for another. When in doubt the best plan is to test the sensitiveness of the patient with small doses, say 10 mgm., and establish the maximum tolerated dose. It is only by experience and judgment that these side-reactions can be reduced to a minimum. According to the experience of early investigators, a single dose of 50 to 100 mgm. for an average adult may be given with safety. Hess advocates the use of 1 to 2 mgm. per kilogramme of body weight, but this dose appears to be somewhat large for ambulatory patients. Our own experience indicates that in uncomplicated cases 25 to 30 mgm. ($\frac{1}{2}$ grain) is sufficient to relieve the paroxysm if the drug is going to act at all and if necessary the dose may be repeated two or three times during 24 hours. In complicated cases with secondary bronchial infections, a slightly larger dose may be necessary, i.e., from 60 to 75 mgm. (1 to $1\frac{1}{2}$ grains), and it is not advisable to overstep these limits. In cases which are not of an allergic nature and which are suffering from secondary bacterial infections and other complications such as emphysema, myocarditis, hypertension, albuminuria, etc., ephedrine, though helpful, does not relieve the condition satisfactorily, and it is no good increasing the dose in the hope of getting better results. Arteriosclerotic changes and permanent hypertension have been experimentally produced in rabbits by repeated injections of adrenalin over prolonged periods. Ephedrine

is a sympathomimetic drug belonging to the same class and has a very similar physiological action. When prescribing the drug to patients for indefinite and prolonged periods this should be borne in mind.

Summary

1. Ephedrine is a powerful drug and should be used with caution.
2. The toxic symptoms met with in patients in the authors' experiences have been described in detail.
3. In patients with high blood pressure, cardiac damage and history of anginal attacks ephedrine should not be given. In diagnosing cases of asthma, great care should be taken in separating cardiac asthmas from bronchial asthmas.
4. Ephedrine is quite effective in doses of $\frac{1}{2}$ to 1 grain (30 to 60 mgms.). In adults this dose can be repeated. The cases not relieved by such doses are not suitable for ephedrine treatment.
5. If during the administration of ephedrine, the patient exhibits any toxic symptoms such as palpitation, tachycardia, arrhythmia and vasomotor disturbances, the drug should be discontinued at once. Indiscriminate use of the drug may lead to serious results.

REFERENCES

- Anderson, W. D., and Homan, C. E. (1927). *Amer. Journ. Med. Sci.*, Vol. CLXXIV, p. 738.
- Althausen, T. L., and Schumacher, J. C. (1927). *Arch. Intern. Med.*, Vol. XL, p. 851.
- Bloedorn, W. A., and Dickens, P. F. (1928). *Arch. Intern. Med.*, Vol. XLII, p. 322.
- Chen, K. K., and Schmidt, C. F. (1924). *Proc. Soc. Exper. Biol. and Med.*, Vol. XXI, p. 351.
- Chen, K. K., and Schmidt, C. F. (1924). *Journ. Pharm. and Exper. Therap.*, Vol. XXIV, p. 339.
- Chen, K. K., and Schmidt, C. F. (1925). *China Med. Journ.*, Vol. XXXIX, p. 982.
- Chen, K. K., and Schmidt, C. F. (1926). *Journ. Amer. Med. Assoc.*, Vol. LXXXVII, p. 836.
- Chopra, R. N., Dikshit, B. B., and Pillai, K. V. (1929). *Indian Med. Gaz.*, Vol. LXIV, p. 1.
- Chopra, R. N., Dikshit, B. B., and Pillai, K. V. (1929). *Indian Journ. Med. Res.*, Vol. XVI, p. 780.
- Chopra, R. N., and Dutt, A. T. (1930). *Indian Journ. Med. Res.*, Vol. XVII, p. 647.
- Chopra, R. N., Ghosh, N. N., and Ratnagiriswaran, A. N. (1929). *Indian Journ. Med. Res.*, Vol. XVI, p. 770.
- Chopra, R. N., Ghosh, S., and Dutt, A. T. (1928). *Indian Journ. Med. Res.*, Vol. XV, p. 889.
- Chopra, R. N., Krishna, S., and Ghosh, T. P. (1931). *Indian Journ. Med. Res.*, Vol. XIX, p. 177.
- Gaarde, F. W., and Maytum, C. K. (1927). *Journ. Lab. and Clin. Med.*, Vol. XII, p. 1203.
- Higgins, W. H. (1929). *Journ. Amer. Med. Assoc.*, Vol. XCII, p. 313.
- Middleton, W. S., and Chen, K. K. (1927). *Arch. Int. Med.*, Vol. XXXIX, p. 385.
- Miller, T. G. (1925). *Amer. Journ. Med. Sci.*, Vol. CLXX, p. 157.
- Pennetti, G. (1928). *Medicine*, Vol. IX, p. 63.
- Pollak, L., and Robitschek, W. (1926). *Wien. klin. Wchnschr.*, Vol. XXXIX, p. 753.
- Thomas, W. S. (1926). *Amer. Journ. Med. Sci.*, Vol. CLXXI, p. 719.
- Wu, S. T., and Read, B. E. (1927). *China Med. Journ.*, Vol. XLI, p. 1010.

BRONCHOSCOPY IN ASTHMA AND OTHER CASES

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CECIL (1930) states that, 'Asthma is produced by a narrowing of the lumen of the bronchi probably throughout the entire bronchial tree, either by spasm of the bronchial muscles or by œdema of the bronchial mucous membrane or both'. He also states that, 'Adrenalin chloride injected subcutaneously can control almost any attack for a time varying from minutes to hours'. This is the accepted view of the pathology and primary treatment. Of course, as he states, the underlying causes are many and are to be sought out and eradicated. Occasionally, however, we find a case which is apparently unaffected by the subcutaneous injection of adrenalin chloride. And in this type of case bronchoscopy has given brilliant results. Moore (1925) studied, histologically, sections of the bronchial mucous membrane of asthmatics who had come to autopsy. In many of these sections there was an absence of cilia, which meant that mucus accumulated in the bronchi could not be readily and naturally expelled. Jackson says, 'In cases studied bronchoscopically during an attack, the bronchi were found filled with tenacious bubbling secretions..... The secretions were removed (by aspiration) and the attack quickly subsided. In many cases a complete cure resulted, in a few others little or no influence on the recurrence of attacks was observed'.

Our first opportunity to try this treatment came in the form of a coolie who had travelled a long distance. He was a Marathia, aged 35 years, who said he had been suffering from cough and dyspnoea for one year. The salient features of the physical examination were two loose teeth, which the patient refused to have extracted, a barrel chest, a few râles at the bases and intense dyspnoea. He was admitted and treated with adrenalin injections, calcium lactate powders and a mixture containing potassium iodide, ammonium bromide, lobelia and stramonium. At the end of two days there was practically no improvement and he consented to bronchoscopic aspiration. During this procedure, the bronchial mucous membrane appeared slightly paler than normal and a small amount of thick tenacious mucus was aspirated from the main bronchi and from the principal branch bronchi.

The patient had a quiet night and the next morning I found him sitting up in bed, and saying that he had not been so comfortable for a whole year. He was discharged the third morning thereafter. This bronchoscopic aspiration was done in January and he was so grateful that I believe he would have returned in case of a recurrence.

During the year ending 1st May, 1933, we have had twenty-three cases where endoscopies on the food and air passages have been performed. They are classified as follows:—

Bronchoscopies for exploration and aspiration	13
Bronchoscopy for foreign body, a tamarind (chinch) seed in the right main bronchus	1
Laryngoscopies, exploratory or for biopsy or removal of tumours from the lower pharynx and larynx	5
Œsophagoscopies, exploratory or for biopsy or treatment of stricture of the œsophagus	4
TOTAL	23

Three interesting cases of the year beside that of the patient suffering from asthma are reported as follows:—

I. U. C., a Goanese hotel proprietor, aged 50, was admitted to the hospital on 28th November, 1932, with a history of fever, cough, foul expectoration and weakness. The symptoms began 21 days before admission with chills and blood in the sputum. Over the lower lobe of the right lung there was marked dullness, also coarse bubbling râles, distant breath sounds and coarse friction rubs. An x-ray plate could not be taken at the time but it seemed clear that the case was that of a lung abscess of the lower right lobe.

On bronchoscopic examination thick pus was found in the right main bronchus. About three ounces of this was aspirated. Then when the aspirating tube was pushed farther down into a branch bronchus, suddenly there was a rush of fluid and twenty-two ounces of watery blood-tinged fluid was aspirated. The most likely explanation of this seems to be that after aspirating the abscess cavity the aspirating tube punctured the lung and the blood-tinged fluid was from the right pleural space. Disastrous sequelae were anticipated but after the procedure the patient's temperature steadily declined and he regained strength. The cough continued troublesome and there was a moderate amount of sputum, but it was no longer foul. After seventeen days, bronchoscopic aspiration was again performed and only half an ounce of pus-like secretion was aspirated. The patient made a slow but steady recovery and was discharged on the 7th February, seven weeks after the second bronchoscopy. He had gained 13 pounds.

II. K. M. B., a man of 40 years, complained of hoarseness of two months' duration. Mirror laryngoscopy showed a tumour of the right arytenoid cartilage, a fullness in the region of the right false cord, hyperemia of both cords with almost complete paralysis. There was residual saliva in the pyriform sinus. Externally there was no palpable glandular enlargement. The larynx could be moved freely but with slight pain. The Kahn test was ++ and anti-syphilitic treatment was begun immediately. But since there is always the possibility of epithelioma of the larynx being coexistent with syphilis, a direct laryngoscopy with the Jackson laryngoscope was performed. A picture similar to the above, but clear, was seen. There was no sign of ulceration but the right arytenoid cartilage was markedly enlarged and hyperemic. The right cord was completely paralysed, the left almost completely. A portion of tissue was removed for pathological examination. This showed no evidence of epithelioma and the anti-syphilitic treatment was continued. The hyperemia and swelling of the right arytenoid rapidly diminished but the paralysis of the cords continued. Here the

(Continued at foot of next page)

SPREAD OF CUTANEOUS LEISHMANIASIS ALONG LYMPHATICS

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CAPTAIN, I.M.S.

and

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CAPTAIN, I.M.S.

A SEPOY, Gurkha, aged 19, was admitted to hospital on 25th February, 1933, with a chronic ulcer on the dorsal aspect of the left middle finger and a similar one on the back of the right thigh.

Past history.—The patient was in hospital with the same complaint in January 1933, when he was given a course of 2 per cent tartar emetic, after which he improved and was discharged from the hospital in the middle of February.

On admission, he showed a large oriental sore of typical appearance on the dorsum of the left middle finger near its base and another on the back of his right thigh. Scrapings from these showed Leishman-Donovan bodies. On the dorsum of the left hand, he also showed numerous small hard painless nodules which he first noticed on 22nd February, 1933.

During his stay in the hospital new, hard and painless nodules continued to appear on the back of left forearm and a few along the basilic vein in the lower part of the arm. These

(Continued from previous page)

result of the biopsy taken by means of the direct laryngoscope gave us confidence that we were dealing only with syphilis and were not delaying during the growth of an epithelioma.

III. E. F., a widow, of 55 years, complained of pain in the neck below the cricoid cartilage, and of being able to swallow only liquids during the three weeks prior to admission. A mirror examination of the larynx was negative. The Kahn test was negative and there was no other evidence pointing to syphilis.

Upon œsophagoscopic examination the cricopharyngeus muscle was passed with difficulty and just below this a stricture of the œsophagus was found. The œsophagoscope passed this stricture however and entered the stomach with no other abnormality being discovered. Three days later a Plummer hydrostatic œsophageal dilator was passed and the water pressure raised until the dial indicated ten pounds pressure. The patient could endure this dilatation for only about 15 seconds because of fright at threatened suffocation. (The rubber bag of the dilator in this case covered the entrance to the larynx.) However, after the procedure she was able to swallow solids and felt so much relieved that she requested two more hydrostatic dilatations at three-day intervals. She left the hospital evidently completely cured and has not been heard of since.

REFERENCES

- Cecil, R. L. (1930). *A Textbook of Medicine*. Second Edition. Philadelphia: W. B. Saunders Company.
Moore, W. F. (1925). Ciliary Inhibition or Destruction in Tracheobronchial Asthma, with Notes on Bronchoscopic Treatment. *Amer. Journ. Med. Sci.*, Vol. CLXIX, p. 799.

nodules were not fixed to the skin and were distributed along the course of the lymphatics. The axillary glands were not enlarged. The accompanying illustration shows the nodules on the back of the hand and forearm. Blood Wassermann reaction was negative.



Illustration showing the ulcer on the finger and the nodules on the hand and forearm.

Some of the nodules on the back of the hand softened gradually. On puncture 2 to 4 cubic centimetres of turbid fluid was withdrawn from each nodule which on direct smear showed Leishman-Donovan bodies, but no other organisms. Cultures on bacteriological medium were also sterile.

One of the nodules on the forearm was excised. On section it showed fluid as described above. Microscopically granulation tissue was seen. No Leishman-Donovan bodies, however, could be detected.

A few of the nodules on the dorsum of the hand ulcerated.

Treatment.—The patient was given a course of 10 injections of neostibosan intravenously: total dose of 2.5 grammes. During the course of injections there appeared to be no effect on the nodules most of which, however, disappeared within a week of the last injection. The ulcers had dried up and nearly healed when he was discharged.

No similar nodules were seen or felt in the vicinity of the ulcer on the thigh.

Conclusions.—Apparently the spread of leishmaniasis in this case occurred along the lymphatics, presumably by permeation along these channels. This mode of spread is considered worthy of note.

We wish to thank Lieut.-Colonel J. F. James, I.M.S., Officer Commanding C. I. M. H., Razmak, for permission to investigate this case.

(Note.—The spread of the leishmania infection along the lymphatics in cases of oriental sore has often been noted before, but the occurrence is certainly of sufficient rarity to warrant publication of this note.—EDITOR, I.M.G.)

ANIMAL PARATYPHOID IN GUINEA-PIGS

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THE following investigation of an outbreak of animal paratyphoid among the guinea-pigs of this laboratory may be of interest to other laboratory workers.

Housing, feeding, etc.—The pigs are housed in two separate rooms on which a run abuts, the rooms being used alternately every other day. Owing to the heavy rains at Maymyo the animals spend most of the time inside (at any rate this applies to the period during which the outbreak occurred).

The animals are fed twice daily on a diet of bran, oats, *gram* and vegetable peelings in lieu of lucerne grass; the peelings are supplied daily by a contractor and procured by him from the local market. Bedding in the shape of dry grass is supplied nightly. The number of guinea-pigs at the end of October was about 150, the animals being somewhat overcrowded.

The outbreak

The first casualty occurred in late October—a rather old pig—and presuming this to be just a case of death from old age we took no action. In the light of further happenings, how grave an omission this proved to be will readily be seen, and will go to show the importance of carrying out a post-mortem examination on all animals dying of an unknown cause, as it is not unreasonable to presume that this was the start of the epizootic.

Within a couple of days of this first casualty, it was noticed that most of the animals were off their feed, being rather lethargic with somewhat ruffled coats; very heavy rain was registered at this time. On the third of November three more pigs died and several others were very ill indeed. From this day onward between two and eight animals died daily, and in spite of every endeavour on our part to stop the outbreak, this state of affairs continued unabated up to the third week of November, when it more or less abruptly ended, leaving us with but seventy pigs—a loss of eighty animals in a period of three weeks.

Post-mortem and cultural findings

On two of the three animals that died on 3rd November post-mortem examinations were carried out; both revealed peritoneal exudates with deep congestion of the small intestines and greater curvature of the stomach, the small intestine showing ulceration and patches of hæmorrhage in the ileum (probably inflamed Peyer's patches). The liver and spleen were congested as also the lungs; there were no signs of scurvy and the suprarenals were somewhat anæmic. A culture was made from the heart's

blood and in both cases *B. enteritidis* was isolated. Post-mortem examinations were carried out on over thirty animals in all, and, with few exceptions, all showed the same morbid changes in varying degrees. Cultures of the heart blood were made in ten cases; five were positive, three were contaminated and no serious attempt was made to recover the organism from these, and two proved to be sterile. In all positive cultures an abundant growth was noted within twenty-four hours. Glucose broth was initially used, but ordinary nutrient broth gave as good results. The ulcerated patches from the intestines in three cases were washed in saline and the washings plated on litmus lactose agar, innumerable colonies of *B. enteritidis* were isolated from these plates. Cultures made from the fæces and stomach contents were less successful for, after many attempts, only one plate proved to be positive; nor could we isolate the organism from the fæces of any sick animal; this appeared to us strange, considering that the utmost care in technique was observed and in most cases only samples that appeared fresh were used. Blood cultures from the hearts of sick animals were more successful, for out of six cultures taken three were positive.

Serological findings

(a) *Guinea-pigs.*—The sera of four animals were taken post mortem and put up against emulsions of *B. enteritidis*, isolated from previous cases; all gave agglutination in dilutions varying from 1 in 50 to 1 in 250.

The sera of three sick pigs were also tested for agglutinins; two gave agglutination in dilutions of 1 in 125 and 1 in 250, the third showed no agglutination. All three animals died later showing characteristic post-mortem changes and from the heart blood of one of them *B. enteritidis* was isolated. Two healthy animals were also tested, but failed to show any agglutinins; it is of interest that these two tests were carried out early in the outbreak. Later, a pooled serum (that used as complement for the Wassermann) was put up and gave agglutination in a dilution of 1 in 250; naturally these sera were from apparently healthy animals. Two healthy animals, tested later still, gave similar results; this would suggest that almost all the pigs were affected to some degree and had developed immunity; but we must here state that—with one exception—every animal that showed signs of being ill died.

(b) *Rabbits.*—The serum of two rabbits housed with the guinea-pigs was also tested; both gave total agglutination in dilutions of 1 in 250. This would appear to bear out our opinion that rabbits are either naturally immune or readily acquire an immunity; but it is only fair to state that these tests were also carried out at the tail end of the outbreak. None of the rabbits, however, appear to have been infected.

(c) *Sheep*.—The sera of two sheep belonging to the laboratory, but housed quite separately, failed to reveal the presence of any agglutinins. All serological tests were controlled as a routine but no auto-agglutination was observed.

Course of disease

The course of the disease was between 4 to 10 days, the first appreciable symptom being an absolute loss of appetite, the animal soon took to a corner where he sat with ruffled fur evincing no further interest in life. Within a couple of days the animal appeared very ill indeed and its condition might well be compared to the typhoid state in man. Diarrhoea was absent in most of the cases, which was strange in view of the post-mortem findings. A few cases developed paralysis of the hind legs, subsequent post-mortem examination in those cases revealed no signs of scurvy. Pregnant females aborted.

Source of infection

The probable source of infection was the vegetable-peeling supply. Cultures were made from the scrapings and washings of peelings supplied, but in no case were we successful in isolating the organism. The spread of the infection was enhanced by overcrowding, rendered worse by the inclement weather at the time, causing the animals to be huddled together for the greater part of the day.

Preventive measures

These consisted of daily flushing out of rooms and run with cresol, spraying the walls and shelves with a solution of formalin—a Flit sprayer being used for the purpose, segregation of all sick animals, burning of bedding, excreta, corpses, etc., and washing all vegetables with a solution of permanganate.

Feeding experiments

In order to study the disease further two guinea-pigs were fed on cultures of *B. enteritidis*. One of them was given a drop from a saline washing and the other a platinum loop from an agar slope; this was done on two consecutive days, but not concurrently. The incubation period would appear to be from two to four days, and the symptoms the same as those previously described. The organism is apparently much attenuated in culture for both animals survived. Prior to the experiment the sera of both animals were tested for the presence of agglutinins; the first showed agglutination in a dilution of 1 in 50, the second was negative. In the first experiment a blood culture was not taken when the pig was ill, as we intended doing this when the animal died; the heart's blood taken later (10th day) when the animal was recovering was sterile. In the second case, profiting by our previous experience, a blood

culture was taken on the fifth day of disease and was positive, the serum causing agglutination in a dilution of 1 in 25. Repeated examinations of the faeces in both cases were negative, and in neither case was there any evidence of diarrhoea.

The following is a daily record of the second guinea-pig; the course of the disease in the first was very similar.

11-11-1932.	590 grammes.	Serum giving no agglutination.
12-11-1932.		Fed with an inoculated platinum loop from agar slope.
13-11-1932.		Do.
15-11-1932.		Ruffled fur. Loss of appetite.
16-11-1932.	550 grammes.	Looks ill.
17 & 18-11-1932.		Very ill. Faeces negative.
19-11-1932.	530 grammes.	Blood culture positive, agglutinins present 1 in 25.
21-11-1932.		Looking better. Faeces negative.
22-11-1932.	560 grammes.	Improving, eating well.
24-11-1932.	570 "	
26-11-1932.	570 "	Appears well.
28-11-1932.	580 "	
30-11-1932.	590 "	Released, quite well.

The following points appear to us of special interest:—

1. The severity of the infection and high mortality; at the commencement of the outbreak we had 150 pigs, and in the course of three weeks this number was reduced to 70. Of the naturally-infected animals, all but one succumbed.

2. The preponderance of deaths among the female pigs; the proportion of females to males affected was about 5 to 1, and we were left with only 5 females at the end of the outbreak. Without exception, all pregnant pigs aborted.

3. The apparent absolute immunity of rabbits; over 20 rabbits were housed together with the pigs under identical conditions, not a single animal was affected; they flourished and bred quite happily in spite of the fact that scant attention was paid to them at the time.

4. The apparent immunity of young pigs; at the commencement of the infection we had 30 young pigs housed in a separate cage. They did well, only two dying during the period, strange to say, both females; post-mortem examinations carried out on these animals did

not reveal any morbid lesions, nor could we isolate any organism from the heart's blood.

The milk of infected animals would appear not to be infective. Two full-term litters, of two each, lost their mothers on the fourth and

fifth days respectively. An attempt to rear them on diluted cow's milk was of no avail, all four dying within a week. Post-mortem examinations carried out on these animals failed to show any characteristic lesions and their heart's blood was sterile.

A Mirror of Hospital Practice

A CASE OF DYSIDROSIS TREATED BY CALCIUM

By S. R. INGLE

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Dysidrosis is a common disease, occurring in young people mostly in the heat of summer, and the usual methods of treatment adopted for this condition appear to be unsatisfactory. The results obtained in the case reported below are thought to be of sufficient interest to justify publication.

Case record

An otherwise healthy Mahomedan boy, aged about 20, consulted me on 10th March for eruptions of about a month's duration on the palms of his hands and toes. For the last four years, he has been suffering from these eruptions which come on every summer, are preceded by a sensation of itching and tingling, and which disappear spontaneously at the approach of the cold season. He always suffers from somewhat excessive perspiration of the hands and feet. There is nothing of importance as regards his past or family history.

When first seen on 10th March, he had symmetrical eruptions, consisting of vesicles and bullæ over the palms of his hands, the sides and webs of the fingers and to a less extent on the toes. Some of the blisters were discrete whilst others had coalesced forming large bullæ, and if one of them was punctured, it exuded slightly turbid fluid, exposing a tender and raw surface. The boy complained of pain, tenderness and itching and consequently suffered from sleeplessness. There were no constitutional symptoms. Physical examination was negative.

Treatment.—During the first four days, the patient was given twenty minims of dilute hydrochloric acid, well diluted in water, and five-grain salol powders, thrice daily after meals. Locally a lotion containing liquor plumbi subacetatis fort., zinc oxide and calamine was ordered; but this gave him no relief. During the next four days, calcium lactate in 10-grain doses thrice daily was tried without any benefit. In the second week, four intravenous injections each consisting of one gramme of calcium gluconate in ten cubic centimetres of water were given and the following lotion and ointment was ordered for local use:

R Liq. plumbi subacetatis fortis.

Liq. carbonis detergentis .. aa. ʒi.

Aquam ad ʒxii.

Sig.:—To be used frequently for cleansing hands and feet.

R Calaminæ preparatæ

Zinci oxidi aa. gr. xxx.

Hydrargyri ammoniati gr. x.

Paraffinum molle ad ʒi.

Sig.:—To be rubbed well in at bed time.

INTESTINAL OBSTRUCTION RELIEVED BY ATROPINE

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FOLLOWING the reports in the *Indian Medical Gazette* of the successful reduction of strangulated hernia after atropine injection I have used it in the two following cases with excellent results:—

INTUSSUSCEPTION

Case 1.—A Mahomedan boy, aged about 12 years, had suffered from intermittent pain in the abdomen for a week. There was a sausage-shaped mass about three inches in length situated transversely in the transpyloric line. The mass changed its position on standing and lying and appeared to be connected with the transverse colon. It could also be made to move up and down by manipulation. During this time the boy passed very little stool, but blood and mucus were passed several times a day and there was considerable tenesmus. The abdomen was not much distended and there was slight tenderness over the tumour. The patient had occasional attacks of vomiting and there was visible peristalsis in the abdomen. The case was diagnosed as intussusception of the transverse colon. A soap-and-water enema was given and the fluid was heard by the stethoscope to flow up to the tumour. The enema was returned and the tumour remained unchanged, but the abdominal pain rather increased. Atropine sulphate 1/100 grain was injected and after three hours the pain disappeared. Twelve hours later I went to see the patient and found that the tumour had already disappeared.

STRANGULATED HERNIA

Case 2.—A Hindu male, aged about 45 years, had had an inguinal hernia on the left side for a long time. Up to the present occasion he had always been able to reduce it himself, but this time he neglected it for some time and then found he could not reduce it.

Taxis was unsuccessfully tried by another practitioner and after about twelve hours I was called to see the patient and found a left inguinal hernia of the size of a big mango. It was very painful on pressure and there was no impulse on coughing. The patient was in

great distress and his pulse was weak and quick. I tried taxis but failed. Atropine sulphate 1/50 grain was then injected hypodermically and Goulard's lotion applied over the herniated mass, and a hot compress over the inguinal canal. In fifteen minutes the pain had disappeared and the patient fell asleep. The hernia gradually became reduced and after six hours it had completely disappeared.

EIGHT CASES OF PLAGUE TREATED WITH 'BAYER 205'*

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Medical Officer of Health, Municipal Borough, Bijapur

In the last plague epidemic of 1932-33 the routine treatment of plague cases at the Municipal Infectious Diseases Hospital was intravenous iodine and a stimulant mixture. After reading the successful results with 'Bayer 205' reported by Dr. B. R. Ranganatha Rao, L.M.P., in the *Indian Medical Gazette* of November 1932, I treated the following eight cases at the hospital by this method. All of the patients were given an intravenous injection of 'Bayer 205' in 10 c.cm. distilled water, and an injection of 1 cubic centimetre of 1/1000 adrenalin on the day of admission. In addition they had a stimulant mixture, were kept in bed on a milk diet, and had belladonna plasters applied to the buboes.

Case 1.—Hindu male, aged 55. History of two days' illness. Removed from his house to hospital on 6th December, 1932. On admission his temperature was 103°F., pulse 135 of low volume and easily compressible and respirations 25. He had diarrhoea the previous day. Tongue—partially paralysed and dry; speech—not clear, delirious at night. There was a tender bubo in the right groin. The next morning the temperature fell to 100.5°F. and pulse to 90 and it was of fairly good volume, and he had no delirium the previous night. On 8th December, 1932, he was given 1 c.cm. adrenalin injection and stimulant mixture and there was no change in his condition as his temperature was 100.5°F. and pulse 100. His relatives were unwilling to keep him in the hospital and so he was removed to his house on the evening of the same day. I examined him in his house on 9th December, when he had a temperature of 103°F., pulse—140 and respirations—30. On 10th December he had a temperature of 104.5°F., irregular pulse—145 and respirations—50. He died on 11th December at 9 A.M.

Case 2.—Mahommedan female, aged 30. History of illness—three days. Removed to hospital on 7th December, 1932. On admission her temperature was 102.5°F., pulse—20 and respirations—20. She was conscious and her speech was clear but her eyes were congested. There was a tender bubo in the left axilla. Next day her temperature came down to 99.5°F. and pulse to 90. She was given 1 cubic centimetre of adrenalin injection and routine stimulant mixture. But on 9th December the disease took a serious turn and she had a temperature—103°F., pulse—120 and respirations—24. Her pulse became rapid and irregular and respirations were 45 on 10th December although her temperature was 100.5°F. She died on 11th December, 1932.

Case 3.—Mahommedan female, aged 25. History of illness—three days. Removed to the hospital on 8th December, 1932. On admission her temperature was

103.5°F., pulse—135 and respirations—20. There was a tender bubo in the left axilla. Next day her temperature came down to 103°F., pulse—135 and respirations—18. On 14th December her temperature was 99.5°F. with pulse 120 and respirations 20. She had normal temperature on 15th December. Her relatives removed the patient to their home in the evening of 15th December. She died on 19th December, 1932, in her house.

Case 4.—Mahommedan male, aged 55. History of illness—two days. Removed to the hospital on 8th December, 1932. On admission his temperature was 103.5°F., pulse—135 and respirations—20. There was a tender bubo in the right groin. Next morning his temperature was 103°F., pulse—130 and respirations—22. On 14th December his temperature fell to normal, and he was discharged cured on 15th December, 1932.

Case 5.—Hindu female, aged 30. History of illness—three days. Removed to the hospital on 20th December, 1932. She was unconscious; eyes—congested; temperature was 105°F., pulse—145, irregular, and respirations—45. There was a tender bubo in the right groin. She died the same night.

Case 6.—Hindu female, aged 30. History of illness—two days. Removed to hospital on 4th January, 1933. There was a tender bubo in the right groin. Her temperature was 103°F., pulse—140 and respirations—30. Next day she had the same temperature but respirations were 35. On 7th January her temperature was 104°F., pulse—145, irregular, and respirations—55. She died in the evening of the same day.

Case 7.—Hindu female, aged 15. Removed from the jail premises to the hospital on 11th January, 1933. Her temperature was 103°F., pulse—150, respirations—25. Next day her temperature came down to 100°F., pulse—130 and respirations—25. But on 15th January the temperature rose to 105°F., pulse—140 and respirations—40. Her lungs showed signs of patchy consolidation. She was given a six-gramme camphor injection in the morning and six grammes in the evening. On 17th January her sputum was rusty, temperature—104.5°F., pulse—150, irregular, and respirations—55. Her relatives removed her to her village 12 miles away, where she died the next day.

Case 8.—Jain male, aged 40. History of illness—two days. Partial paralysis of tongue. Eyes—congested. Admitted to hospital on 13th January, 1933. His temperature was 105.5°F., pulse—140 and respirations—30. Next morning his temperature was normal with pulse 120 and respirations—25. Till 18th January he had a normal temperature and pulse—100 but respirations increased to 30. On 19th January he lost the power of speech, the tongue became dry, temperature—98°F., pulse—100 and respirations—40. On 21st January, 1933, his pulse became rapid and irregular and respirations—55, and he died in the evening of the same day.

Only one out of eight persons treated by 'Bayer 205' recovered, therefore the drug does not appear to be of much use. At the same time it should be stated that most of the patients had severe pneumonic complications, so it is not possible from these results to express an opinion on the value of 'Bayer 205' in uncomplicated bubonic plague.

CONGENITAL ABSENCE OF THE EYES*

By P. R. PRABHAKAR

State Hospital, Mirpur (Jammu State)

In the course of out-patient work in the above hospital a child aged two months was shown

* Rearranged by Editor.

* Rearranged by Editor.

to me by the mother, who gave the history that it had never opened its eyes. At first it seemed that the two eyelids were adherent, but on further examination it was found that they were retracted and that both eyes were completely absent. This condition must be extremely rare because I have not been able to find any mention of it in the books at my disposal.

I wish to thank Dr. Fazel Rahman for permission to publish this note.

[Note.—Professor M. N. De, Professor of Pathology, Medical College, to whom we showed the above report, has kindly supplied us with the following note on this condition:

Complete absence of the eyes, which is usually a bilateral condition, is met with in healthy well-developed children, and is often associated with other malformations, such as hare lip, supernumerary digits, etc. As a rule, the eyelids are well formed but may be adherent at the margins. The orbit is usually smaller than normal and is lined by conjunctiva. In all such cases, digital examination will reveal either a cystic or a hard mobile nodule at the extreme apex. The lacrimal gland is usually present. The nodular mass is composed of the subsidiary parts of the eye derived from the mesoblastic elements. There is, however, a complete absence of the essential nervous elements constituting an eye.

This condition, though very rare, is occasionally met with in the out-patient clinics of any big hospital and is a well-recognized form of developmental anomaly of the eyes.—EDITOR, *I. M. G.*

SPASMODIC STRICTURE OF THE GULLET

By M. A. KRISHNA IYER, L.M.P.

Medical Officer, Tirutani, Chittoor District

The following case seems worth recording:—

A woman, aged about 30, was brought to me with a history of some difficulty in swallowing. She was partaking of dinner at a marriage party at 11 p.m., when suddenly, at the end of the meal, she thought she swallowed a big ant or beetle when drinking water. Immediately she felt a choking sensation. She tried to drink more water but could not swallow a drop. Many attempts to force water down her throat not only failed but produced an intense feeling of suffocation. She was brought to me at about 11-30 p.m. I gave her a cup of water and asked her to sip, but she could not swallow and the few drops of water practically choked her. By means of an electric torch I examined the throat and found nothing abnormal. I introduced my finger and inserted it as far as it would go, and found no obstruction. The patient appeared to be of a nervous temperament. When asked to shut her mouth firmly and breathe through her nose, she did so for about five minutes without feeling any discomfort. I brought a rubber tube and told her that I was going to introduce it into her mouth and push the obstructing material down. She tried to resist, but her relatives held her firm. Though I tried many times I could not put the rubber tube through the mouth. Therefore I introduced it through her nose. When the tube had gone in about one foot, she began to cry out and say that she was better and that the tube could be removed.

I removed the tube and gave her a cup of water. She drank it freely and asked for more, which was given. She was taken home quite recovered.

The points for note are:—

(1) She could not swallow even a drop of water.

(2) The act of swallowing apparently sent the water into the trachea and hence produced a feeling of suffocation.

(3) The symptoms were real and not feigned.

(4) The tubing went in freely and there was no obstruction felt.

(5) Though nervous, she could not be considered hysterical.

On these grounds I made a diagnosis of spasmodic stricture of the oesophagus.

AN UNUSUAL STRANGULATED HERNIA

By C. H. REINHOLD

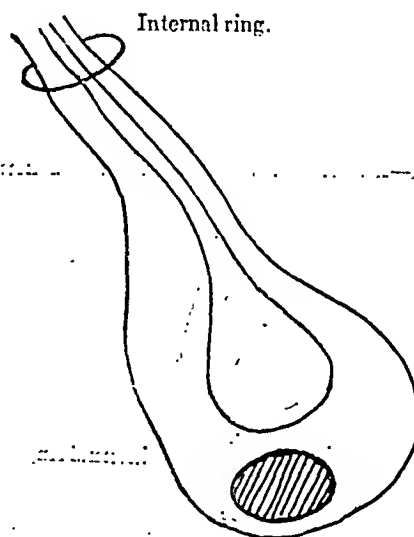
LIEUTENANT-COLONEL, I.M.S.

Civil Surgeon, Lucknow

PURBU DIN, aged 35, a Parsi villager had an inguinal hernia of several years duration which became strangulated about the end of April. After eight days of harsh village treatment his serotum ulcerated and relief came with the formation of a faecal fistula. He was admitted into the Bahampur Hospital on 4th May, two days after.

He was very emaciated and showed marked toxæmia and the surroundings of his wound were unhealthy. After feeding and cleaning him up for a few days to improve his condition, I

Fig. 1.—Faecal fistula in serotum.



decided to do a lateral anastomosis above the herniated loop, and this was effected through a para-rectal incision on 15th May; the hernia was of the small gut. The patient made an uninterrupted recovery, the wound healing by first intention; but unfortunately, the faeces continued to pass through the fistula.

A second operation was done on 24th May, through an incision along the upper half of the inguinal canal, the herniated loop in the canal was cut across and an end-to-end anastomosis of the two upper ends of the gut was effected. This wound also healed without incident, and the bowels at once began to move naturally.

The faecal fistula at once stopped discharging faeces but a small sinus persisted from which mucus exuded, coming from the remnant of bowel left in the sac.

A third and final operation through an inguino-serotal incision was therefore undertaken on 14th June and the loop of bowel was

Fig. 2.—Lateral anastomosis above hernia.

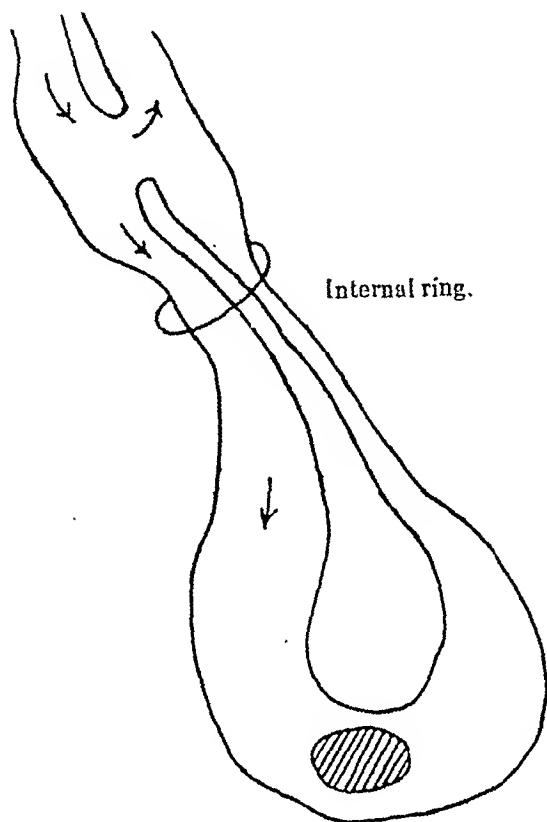
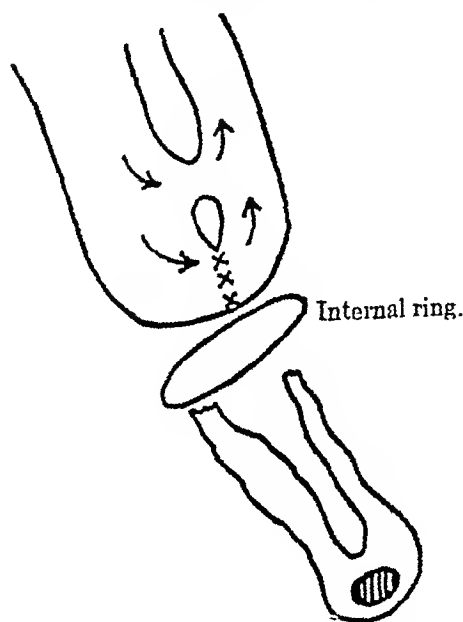


Fig. 3.—End-to-end anastomosis through hernia.



removed without sacrificing the integrity of the cord. The man finally left hospital on 2nd July having put on more than a stone in weight.

All the operations were performed under per-caine spinal anaesthesia and the patient never complained of any headache or caused us a moment's anxiety.

I have to thank my house surgeon Dr. R. S. Gupta, M.R.C.P., for his unremitting attention to the case.

SPINA BIFIDA WITH MENINGO-MYELOCELE*

By A. K. CHANDA, L.M.F. (Bengal)
Medical Officer, Bhikasin Hospital, Almora,
United Provinces

THE following case occurred recently in my practice :—

History.—A child was born with a small swelling the size of a betel nut over the lumbar region of the spine. This gradually increased in size and there was gradual thinning of the skin covering the swelling. At the age of five months it was the size of an orange and was very soft in the centre. A local *vaidya* diagnosed it as an abscess and made a small incision into it. Watery fluid escaped and for the next twenty-four hours the child gradually collapsed. At this stage I was called in.

Examination.—Patient very weak and drowsy, cannot suck the mother's breast. Pulse weak and rapid. The posterior parts of the arches of the 3rd and 4th lumbar vertebrae are absent and the space is occupied by a soft swelling into which an incision has been made; and from the incision, when the patient moves, cerebrospinal fluid escapes. There are bands of adhesions between the superficial covering and the interior of the swelling, dividing the cavity into compartments.

Diagnosis.—Spina bifida with meningo-myelocele.

Treatment.—Disinfection of the surrounding parts, injection of the cavity with 10 c.cm. of normal saline, closure of the opening by sutures, and firm bandaging.

The patient improved for twenty-four hours but on the third day collapse occurred, and the patient died on the fourth day after operation.

A LARGE PEDUNCULATED LIPOMA ON THE NECK*

By J. SATYANARAYANAMURTI, L.M.F.
Sub-Assistant Surgeon (Reserve Duty), Government
Head-Quarters Hospital, Nellore

A MAN aged about sixty was brought to me while I was in charge of a dispensary at Kunavarum, Upper Godavari agency.

He had a large pedunculated tumour situated on the back of the neck. This tumour first made its appearance about forty years ago and since then it had gradually increased in size. The growth never caused any pain and the man had always refused operation. Recently, however, he allowed a friend in his village to open it with a sickle with the idea of letting out the contained fluid. This 'operation' only caused pain and suppuration so the patient came to me and agreed to have the tumour removed.

Under local anaesthesia this was successfully done and the tumour was found to weigh about eleven pounds. On section it appeared to consist of soft fatty material interspersed with dense fibrous tissue.

* Rearranged by Editor.

CORRIGENDUM

THE ANÆMIA OF KALA-AZAR (NAPIER AND SHARMA)

In the above paper, which appeared in the October number of the *Gazette*, on line 7 of the first column of page 553, 'above normal for 24 hours' should read 'above normal for 2½ hours'. From the same paper the following reference was also omitted:—

Meleney, H. E. (1925). The Histopathology of Kala-azar in the Hamster, Monkey and Man. *Amer. Journ. Path.*, Vol. I, p. 147.

Indian Medical Gazette

NOVEMBER

BERI-BERI AND EPIDEMIC DROPSY

BERI-BERI has been recognized as a distinct disease by the Chinese for many centuries, and mention of it is also found in Japanese writings of the seventeenth and eighteenth centuries. Our modern knowledge of beri-beri may be considered to have begun with the work of Bontius in 1642, and in 1835 Malcomson wrote an excellent description of this disease. Epidemic dropsy is probably just as ancient, but it was not until 1877 that McLeod, during a famine in southern India, first suggested that it was different from beri-beri. The controversy raised by McLeod's suggestion has raged fiercely until the present day and there are still some eminent workers who consider that beri-beri and epidemic dropsy are not distinct diseases.

The reason for this confusion is that the epidemiology and symptomatology of the two diseases are very similar. Both are found in races for whom rice is the staple article of diet, and they are both liable to appear suddenly and to affect large numbers of the community in a short space of time. The principal symptoms of these diseases are polyneuritis, œdema and cardiac hypertrophy followed by dilatation of the heart, often acute. Beri-beri may appear either as the 'dry' type in which there are heart lesions but little or no œdema and in which the main symptoms are due to an extensive peripheral neuritis, or it may be the 'wet' type in which œdema is the principal sign and the neuritis is not so marked. Wet beri-beri has a close clinical resemblance to epidemic dropsy and the two conditions may be difficult to distinguish; it is this superficial resemblance that has led to the confusion which is only now disappearing. Close study of epidemic dropsy during recent outbreaks has shown that it differs from beri-beri in that the characteristic peripheral neuritis is absent and that gastrointestinal irritation, a peculiar mottling of the skin, and hæmorrhages from the mucous membranes, none of which are seen in beri-beri, are common symptoms.

Before the advent of modern biochemical methods and the establishment of the fact that vitamins are important ingredients of all diets if health is to be maintained, many theories as to the causation of these diseases were put forward by different workers, and although these theories are of little importance in the light of modern knowledge it may be of interest

to give a brief recapitulation of them to show how we have gradually reached our present state of knowledge regarding the ætiology of these diseases. Calcium deficiency in the blood, diminution in the amount of circulating proteins producing lowered osmotic pressure and consequent œdema, intoxication from a diet of unsuitably-dried fish, and mustard-oil poisoning have each been suggested as causes of the disease, but modern research has not supported any of these theories.

Takaki of the Japanese navy was the first to suggest food deficiency as a cause of beri-beri; he believed that insufficient protein was the factor, but his theory was discounted by the later observation that 'war œdema' appeared to be produced by a diet deficient in fat and not in protein.

The fundamental step in our present knowledge of these diseases and the one on which all subsequent researches have been based was the observation of Eijkman that polyneuritis can be produced in fowls by feeding them on rice with all the pericarp removed by polishing, and that the occurrence of the disease can be prevented, or its cure after it has developed can be brought about, by the addition of rice polishings to the polished rice in the diet. Eijkman was followed by McCarrison and his associates, who produced pure polyneuritis and true beri-beri in pigeons by feeding them on polished rice. Soon after this Stanton, Fraser and Funk, and a little later Braddon, Vedder and Chamberlain brought forward satisfactory evidence that the artificially-produced disease of birds and beri-beri in human beings were essentially the same, and that one cause, at least, of both conditions was the eating of highly polished rice deprived of its pericarp. It was then discovered that the pericarp of rice contained a special factor, now known as vitamin B, and that the absence of this substance which is removed when rice is too highly polished was the cause of the disease. This vitamin is present in many other foods as well as the pericarp of rice, so it is only among races which depend chiefly on rice for their food that the amount of polishing to which it is subjected becomes a matter of importance.

Not long after the above facts appeared to have been firmly established a doubt arose as to their being the complete explanation of the problem, because it was noticed that some rice-eating peoples still developed œdema and its sequelæ at certain seasons of the year, even when they were eating rice with sufficient pericarp adhering to it to prevent beri-beri. Accordingly attention was now directed towards the possibility of rice being harmful in other ways than by deficiency of pericarp alone.

Arguing from the clinical manifestations of epidemic dropsy, which are more like those of a toxæmia than of a food deficiency, and from the fact that outbreaks are often of an explosive

nature such as would be unlikely in food deficiency, Bernard of Saigon, Conton, Leporini, and Wydooghe have formulated the theory that the disease is an intoxication or toxi-infection due to the action of bacteria on the intestinal contents. Megaw, Acton and Chopra, working in the Calcutta School of Tropical Medicine, have had a unique opportunity of studying the epidemics which have occurred from time to time in Calcutta and its adjoining suburb, Howrah, and they consider that epidemic dropsy and some of the conditions occurring in other countries hitherto described as beri-beri are different clinical aspects of a toxic syndrome caused by the ingestion of poisonous bases formed in rice under improper conditions of storage. By studying all the different grades of rice consumed in the localities affected, Acton and Chopra were able to show that the rice grains were definitely diseased and that they were attacked by a spore-forming proteolytic bacterium of the *B. vulgatus* group, which gives rise to poisonous bases from decomposition of the grain. Evidence has also been adduced that these bacteria may act on different grades of rice and produce different amounts of the toxins which cause neuritis and œdema. The views of the Calcutta School have not been universally accepted and criticisms have been levelled at it from time to time. Striking confirmation of the Calcutta

work has recently been provided, however, in another distant part of the world, and elsewhere in this issue will be found a very full abstract of a valuable report from Sierra Leone. Here, Dr. Burnett, following the lines of investigation suggested by the work done in Calcutta, has provided overwhelming proof that epidemic dropsy is a common condition in that colony and that it is caused by the consumption of old and badly-stored rice.

Whatever may be the real position with regard to the identity of the two diseases, beri-beri and epidemic dropsy, there is little doubt that rice dietary plays a very important part in their ætiologies. It is important therefore for nations whose staple food is rice to realize this fact and to adopt stringent preventive measures. These diseases are so serious, they are responsible for such an immense amount of mortality and morbidity, and their prevention appears to be such a simple matter, that Governments of the countries affected might well consider the advisability of formulating regulations for ensuring the proper storing of rice, and for restricting the sale of diseased grain. Such measures, if effectively carried out, would probably stamp out this disease in a very short time, and the drafting and enforcement of a code of regulations on these lines offers a great opportunity for a large scale demonstration of the value of preventive medicine.

Special Article

THE DIAGNOSIS OF THE CLINICAL TYPES OF ASTHMA AND THEIR CAUSATION

By HUGH W. ACTON, C.I.E.

LIEUTENANT-COLONEL, I.M.S.

Director, School of Tropical Medicine and Hygiene
and

DHARMENDRA, M.B., B.S.

Assistant Research Worker, School of Tropical Medicine and Hygiene

WE have divided our cases of asthma into two main groups: (a) cases in which the attacks are secondary to infections of the respiratory tract, i.e., nose, throat and bronchi, and (b) allergic cases. We are of the opinion that a consideration of the personal and family history together with the results of the blood examination will usually enable a case of asthma to be classified into one of these two main groups. An examination of the nose and paranasal sinuses, a skiagram of the chest, von Pirquet's test, and sputum analysis will confirm the diagnosis in the cases in which the attacks are secondary to infection of the respiratory tract. The dermal tests and examination of the

stools will help in the diagnosis of the allergic cases.

In previous papers (1933) we discussed the value of the Arneith count, the eosinophile count and the presence of Gram-negative bacilli in the sputum in differentiating one group from another. An analysis of one hundred and fifty cases has also been published; in this paper we have summarized the procedure which is followed when a case of asthma is admitted into hospital.

1. A history of the case is taken and the following points are carefully inquired into:

(a) A history of inheritance. This is commonly found in the allergic cases and rarely in the bronchial cases.

(b) The pre-asthmatic state. A history of having suffered previously from pneumonia, chronic bronchitis, or pleurisy is very suggestive of the bronchial type, while a history of a previous attack of dysentery or of urticaria is rather suggestive of the allergic type.

(c) Age of onset, the season of incidence and the association of the attacks with eating at a certain place or of a particular food. These are all important points; a history of the disease starting after thirty years of age with attacks

coming on during the winter or rainy season, or being worse at these seasons, is characteristic of bronchial cases. In these cases there is no association of the attack with any place or food. The allergic cases usually start early in life, have no seasonal variation, and the attacks may show an association with some place or food.

2. Examination of the blood. A total leucocyte count and a differential count is done and the total number of eosinophiles per cubic millimetre of blood is calculated. An Arneth count is done along with the differential count:

(a) The total number of leucocytes is not a reliable guide because various diseases in the tropics, such as malaria and kala-azar, lower the count. A high count is suggestive of sepsis and is found in bronchial cases, but when the high count is due to an increase in the number of eosinophiles it is found in the allergic and the Gram-negative-bacilli cases.

(b) The number of eosinophiles. Sometimes the results are difficult to interpret because other causes, such as kala-azar or malaria, depress the bone marrow function. A point to realize is that the results expressed as percentages of eosinophiles are not of much value, because a 5 per cent eosinophilia with a total count of 5,000 leucocytes only means 250 eosinophiles per c.mm., whereas with a count of 20,000 it means 1,000 eosinophiles per cubic millimetre. We now express our results in terms of total eosinophiles per cubic millimetre of the blood. Roughly, an eosinophile count of over 1,000 per cubic millimetre is suggestive of allergy but it is also seen in the Gram-negative-bacilli cases.

(c) The Arneth count: The significance of the Arneth count has been discussed recently by the writers (1933). The points of importance are briefly summarized below:—

In bronchial cases where sepsis is present there is an increased demand on the bone marrow so that young forms are thrown into the circulation at a greater speed than normally. The result of this enhanced supply is that cells with one- or two-lobed nuclei are found in greater numbers than normal—this is spoken of as a shift to the left in the Arneth count. When the Arneth index, which is the sum of the cells with one- and two-lobed nuclei and half the cells with three-lobed nuclei, is above 70, we consider it suggestive of the bronchial group. In the allergic cases there is no sepsis and hence no demand on the bone marrow for the increased production of the polymorphonuclear cells, so that the Arneth index is more or less normal, hence when the Arneth index is below 70 we regard it as suggestive of allergy. It is to be noted that in allergic cases with leucocytosis, although the bone marrow is active, there is no left-handed shift in the Arneth count because the increase in the number of the leucocytes is due to an increase in the number of eosinophiles and not of the polymorphonuclear cells. Thus we see that the combined readings of the Arneth index and the eosinophile count can be divided into four groups (see table):

(a) An Arneth index below 70 and an eosinophile count below 1,000 per cubic millimetre of blood. This group usually contains those allergic cases which have a low eosinophile count.

(b) An Arneth index below 70 and an eosinophile count above 1,000 per cubic millimetre of blood. This

group contains most of the allergic cases and some of the Gram-negative-bacilli cases.

(c) An Arneth index of above 70 and an eosinophile count of below 1,000. This group contains most of the bronchial cases.

ARNETH INDEX

Eosinophiles under	60- below	61-65	66-70	71-75	76-80	81-85	86-90	Above 90
250			2	1	6	5	2	1
500			3	8	3	3	2	
750		1	4	2	1	2	1	1
1,000	1	1	2	5	2	3	4	1
1,500					1			
2,000		1	1	2	1		1	1
3,000	1	1		1	1			
4,000		1			1	1	1	1
5,000	1	1		1		1		
6,000				2	1	1	1	
7,000	1	1					2	
8,000		1	1					
9,000	1		1					
10,000		1		1			2	
11,000					1			
12,000	1		1					
13,000			1					
15,000				1				
16,000			1					1
18,000								
25,000						1		
34,000		1						

The table shows the distribution of the various clinical types of asthma according to their Arneth index and eosinophile count.

Allergic cases are shown in heavy type, Bronchial cases in fine type and Gram-negative-bacilli cases in outlined type.

(d) An Arneth index of above 70 and an eosinophile count of above 1,000. This group contains most of the mixed bronchial and allergic and the Gram-negative-bacilli cases.

Inversely this may be expressed as follows:—

(a) The bronchial cases usually have an Arneth index above 70 and an eosinophile count below 1,000.

(b) The mixed bronchial and allergic cases have an Arneth index above 70 usually with an eosinophile count of above 1,000.

(c) The Gram-negative-bacilli cases usually have an Arneth index above 70 with an eosinophile count of above 1,000.

(d) In the allergic cases the Arneth index is almost always below 70 and is usually associated with an eosinophilia of above 1,000, but the eosinophile count may be low in some cases when the total count is low.

3. *Analysis of the sputum.*—A smear made from the purulent portion of the sputum usually shows the common micro-organisms—pneumococci, streptococci and *Micrococcus catarrhalis*. In 18 per cent of our cases, in addition to these micro-organisms, we found Gram-negative bacilli resembling *Klebsiella pneumoniae* (Friedlander's bacillus). We isolated the last-named organisms from the cultures made from sputa; fourteen out of the fifteen strains studied were non-lactose fermenters, they fermented glucose, maltose, saccharose and usually mannite with the production of acid only. The organisms were very pleomorphic; in cultures coccid and long filamentous forms were seen. No capsule was demonstrated in any instance and the organisms were non-pathogenic to mice, thus differing from *Klebsiella pneumoniae* which they resemble superficially. Out of the fifteen strains studied thirteen belonged to the genus *Eberthella*. In its specific characters the organism is nearest to *Eberthella phaffi*, the causative organism of fowl typhoid, being non-motile, a non-lactose and non-dulcitate fermenter, forming acid in glucose, saccharose and usually in mannite and producing no change in litmus milk and not pathogenic to laboratory animals. Special significance has been attached to the presence of these bacilli in the sputum. Knott and Oriel (1930) obtained histamine-like effects from extracts of various asthmatic sputa. Referring back to the bacteriology of these particular sputa, they found that many showed numerous Gram-negative bacilli in the bronchial plugs. The broth culture of these bacilli has a histamine-like effect similar to that obtained from the sputum. They think that the histamine-like substance demonstrable in the plugs has arisen as a result of the growth of these bacilli within the small bronchial tubes. Oriel (1932) considers that the local production of histamine in the bronchi, in addition to causing contraction of the plain muscle surrounding the bronchi, would also tend to increase the permeability of the epithelium lining the bronchioles, and facilitate the entrance of foreign proteins and possibly of bacteria. We have not succeeded in demonstrating any histamine-like effect in cultures of the strains of the Gram-negative bacilli studied by us. All we can say at present is that the Gram-negative-bacilli cases constitute a clinical group characterized by a high blood eosinophilia and the presence of

pleomorphic Gram-negative bacilli in smears and cultures of the sputum. The benefit in these cases derived from vaccines made from these bacilli is the same as in the other bronchial cases.

We have not found the presence or absence of eosinophiles in the sputum of any diagnostic value. There was no correlation between the sputum eosinophilia and the blood eosinophilia. Out of the total number only 36 cases, i.e., a fourth of the total, had eosinophiles in the sputum. The cases with the Gram-negative-bacillus infection had a higher incidence of sputum eosinophilia than other cases.

4. *The therapeutic test.*—During the attack of asthma, the effects of atropine, aspirin and adrenalin are tried in turn, beginning with atropine, then trying aspirin and after that adrenalin. In some severe cases none of these three drugs gives any relief to the patient and we have to give morphine-atropine injections. A subcutaneous injection of 1/150th grain of atropine sulphate is given at the onset of the attack. Atropine paralyses the vagal nerve-endings in the bronchi, and if the attack is due to broncho-constriction from reflex stimulation of the vagus the injection will relieve the patient. On the other hand if the attack is due to direct chemical stimulation of the bronchial muscles it will have no effect on the attack. Gillespie (1931) by using the method of McDowall and Thornton for recording the movements of the isolated bronchi has shown that the bronchial muscles contract with pilocarpine injection and that a small dose of atropine immediately after this produces complete dilatation; a second dose of pilocarpine then produces no result, but a very small dose of histamine still causes the muscle to contract. Aspirin is given in the form of an A. P. C. powder (aspirin grs. v, phenacetin grs. iii and caffeine citrate grs. iii), and in the bronchial cases we have found it a very effective drug in relieving the spasm. In cases where the broncho-constriction is due to direct chemical stimulation (the allergic cases), the drug has no effect. Clement Francis (1929), discussing the prognosis of operations for removal of nasal polypi in cases of asthma, comes to the conclusion that the removal of polypi will benefit the asthma only if the patient can take aspirin. Probably in these cases the attacks of asthma are due to a reflex irritation from the polypi while in the unrelieved cases the polypus is only a coexisting factor and has nothing to do with the attacks of asthma which are due to some direct chemical stimulation of the bronchial muscle. Van Leeuwen (1931) reporting on the clinical treatment of 1,000 asthmatic patients in allergen-proof chambers states that 10 per cent of his cases were hypersensitive to aspirin and these patients were rarely benefited by residence in these chambers.

Adrenalin.—0.3 to 0.5 c.cm. of adrenalin hydrochloride (1 in 1,000 solution) is injected subcutaneously at the onset of the disease. We have seen that allergic cases are benefited by this injection more than bronchial cases. Adrenalin has no action on the vagus nerve-endings and acts best when the broncho-spasm is due to direct chemical stimulation. Therefore bronchial cases are benefited most with aspirin and the allergic cases most with adrenalin. This forms a good therapeutic test for differentiating these two types of cases.

We next confirm our diagnosis. In the cases due to infection in the respiratory tract we examine the nose and the para-nasal sinuses, try the von Pirquet's test and take a skiagram of the chest. The von Pirquet's test and an x-ray picture are of value in excluding tuberculous lesions of the lung. In our series of 106 bronchial and Gram-negative cases there was radiological evidence of tuberculosis in 18 cases, of these 13 had old healed lesions and 5 active disease. All the bronchial and the Gram-negative-bacilli cases showed enlarged hilus glands and increased fibrosis. The von Pirquet's test was positive in more than half the bronchial and Gram-negative-bacilli cases; a negative test is of definite value in excluding tuberculosis whilst a positive result does not always mean an active lesion; it may be due to an old healed focus.

The diagnosis in the allergic cases is confirmed by the examination of the stools and the results of the dermal tests.

Examination of the stools.—The allergic cases secondary to gut infection may show *Entamoeba histolytica* or the presence of the ova of helminths. The McConkey neutral-red lactose agar plate may show various non-lactose fermenting bacilli suggesting the presence of post-dysenteric lesions. These findings are rather important from the treatment point of view. Cases of gut origin are treated with emetine, carbon tetrachloride or an autogenous vaccine prepared from the pathogenic organisms isolated from the stools, the form of treatment depending on the diagnosis made from stool examination. In the ordinary way these infections do not cause asthma, but there may be a lowering of the defence mechanism of the liver from hepatitis caused by amoebic or some other infection. We are at present investigating the part played by the liver and the endocrine defence mechanism in producing these allergic cases which in India differ so markedly from European cases of the same type.

The dermal tests are of value in the following types :—

(1) When the respiratory mucous membrane is locally sensitive to specific dust, as in jute-mill workers. In 16 cases of asthma tested 10 gave a positive reaction between 1 in 10,000 and 1 in 1,000,000 dilution. Three only reacted at

a dilution of 1 in 100, but out of five controls only one reacted at 1 in 10,000 dilution.

(2) Cases which are sensitive to animal emanations.

(3) Cases in which a single rare food is responsible for the attacks.

In allergic cases dependent on some pathological condition of the gut, dermal tests are of no value, the tests are either totally negative or all the foods tested give a positive result.

Therefore we have discontinued making the dermal test as a routine and only use it when the history is suggestive of some animal emanation or of a particular food being responsible for the attacks.

The dermal tests are usually done on the forearm. The forearm is carefully cleansed with alcohol, and scratches are made on it transversely to the long axis of the arm. The scratches are only about $\frac{1}{4}$ th of an inch in length and they are made without drawing blood. One spare scratch is made to serve as the control. A drop of N/10 sodium hydroxide solution is put on each scratch and the substances to be tested are rubbed into them, one substance into each scratch, the control scratch receives nothing but sodium hydroxide. After 15 to 20 minutes the test fluid is wiped away and the results are read by comparing the site of each scratch with the control. A positive result is denoted by the appearance of an urticarial wheal at the site of the scratch. The materials for testing can be purchased ready-made from the market or they can be manufactured in the laboratory. The supernatant fluid obtained by macerating a small amount of the substance in a few drops of N/10 sodium hydroxide solution may be used for the test, but a better way of preparing an extract for dermal tests is to extract it with Coca's fluid. Coca's fluid is made by dissolving sodium chloride 10 gms., sodium bicarbonate 16.8 gms., and carbolic acid 8 gms. in two litres of distilled water. Before extracting house dust it should be washed in ether to remove the fat and then a 1 per cent extract made in this fluid. The extract should be filtered through a porcelain filter and the filtrate should be tested for sterility (aerobically and anaerobically) before it is used for the test. The test should be performed with very weak dilutions to avoid undesirable effects; it is best to commence testing with a one in a million dilution.

We can define our two groups:

(a) Cases in which the attacks are secondary to infection or disease of the respiratory tract, i.e., nose, throat, trachea and bronchi. This group includes the majority of cases amongst Indians. In our series of 150 cases this group included 70 per cent of them and they can be subdivided into

(i) *Nasal reflex*.—In this type the total leucocyte count is more or less normal, there is

no eosinophilia, and the Arneth count is normal. The cases that respond favourably to aspirin will be benefited by a nasal operation. In such cases an examination of the nose and para-nasal sinuses is carried out.

(ii) Cases in which the attacks are due to pressure of the enlarged hilus glands on the vagus nerve. In such cases there is no increase in the number of total leucocytes or eosinophiles and the Arneth count is more or less normal. The x-ray picture will show enlarged hilus glands.

(iii) Bronchial cases due to infection in the bronchi. These cases are subdivided into two groups :

(1) Gram-negative-bacilli cases. The total leucocyte count is high, there is an increased eosinophilia and a shift in the Arneth count to the left. A smear of the sputum shows the presence of Gram-negative bacilli resembling the pneumo-bacillus. The sputum is cultured and non-motile bacilli belonging to the Eberthella group are isolated. A vaccine is made from these organisms and it is used for treatment.

(2) Bronchial cases in which the infection is due to the ordinary organisms causing bronchitis. The total leucocyte count may be high or low, and there is no eosinophilia but there is a marked shift in the Arneth count to the left. In such cases cultures from the sputum are made to get the strains for preparation of an autovaccine. An x-ray examination of the chest and a von Pirquet's test are done to exclude tuberculous cases.

(b) *The allergic cases.*—There is usually a high leucocyte count and a high eosinophilia and no shift in the Arneth count. These cases may be divided into three groups :

(i) Local allergy of the mucous membrane to foreign substances such as dust. These cases may be congenital or may be acquired as a result of the previous disease of the bronchi. The congenital cases are rare amongst Indians but common amongst Europeans. In India the condition is more often acquired as the result of previous bronchitis. This type is common amongst jute and textile workers and in certain occupations where there is a large amount of dust in the atmosphere. Dermal tests are of value in diagnosing these cases. And they can be treated with extracts made from the specific dust. The treatment is carried out by giving graduated doses of the sterile dust extract.

(ii) Hereditary allergy, i.e., susceptibility to animal emanations. These cases are rare in India. Dermal tests are of value in the diagnosis and the treatment consists in avoiding the excitant or in desensitizing against it.

(iii) Allergy due to internal toxins. This group can be subdivided into two types :

(1) Those due to some rare or common food or foods. Dermal tests are useful in the

diagnosis of these cases, but this type is rare amongst Indians.

(2) Those with allergic symptoms secondary to bowel diseases. These are common amongst Indians and the dermal tests are of no value because either they are all negative or all the foods tested give positive results.

It is interesting to note that the allergic conditions of the skin bear a close resemblance to the allergic conditions of the bronchi. Thus abnormal sensitiveness of the mucous membrane of the bronchi to foreign substances may be well compared to the condition of the skin known as dermatographia, when it is abnormally sensitive to external stimuli, such as scratching. Hypersensitiveness of the bronchial mucosa developing after some disease is comparable to dermatitis venenata which may develop after certain skin diseases. Allergic asthma due to internal toxins may be compared to urticaria which is an abnormal sensitiveness of the skin to internal toxins.

We have divided our cases into two groups—bronchial and allergic, but there are some which are a mixture of the two types. For example if a case starts with bronchial symptoms but later the mucous membrane of the bronchi becomes hypersensitive to dust, or other substance as a result of the disease, it will present a mixed blood-picture, high leucocytosis, high eosinophilia and a marked shift in the Arneth count to the left. Similarly in a case which starts as an abnormal sensitiveness of the mucous membrane to external stimuli, the repeated turgescence of the membrane and its lowered resistance leads to bacterial infection of the mucous membrane, and later the bronchial glands may become enlarged as a result of this infection.

REFERENCES

- Acton, H. W., and Dharmendra (1933). Gram-negative Bacilli isolated from the Sputum in Cases of Asthma. *Indian Med. Gaz.*, Vol. LXVIII, p. 192.
- Acton, H. W., and Dharmendra (1933). An Analysis of One Hundred and Fifty Cases of Asthma. *Ibid.*, p. 185.
- Acton, H. W., and Dharmendra (1933). The Arneth Count with Particular Reference to its Diagnostic Value in Asthma. *Ibid.*, p. 257.
- Acton, H. W., and Dharmendra (1933). The Role of Eosinophiles in the Diagnosis of Spasmodic Asthma. *Ibid.*, p. 436.
- Francis, C. (1929). The Prognosis of Operations for Removal of Nasal Polypi in Cases of Asthma. *Practitioner*, Vol. CXXIII, p. 272.
- Gillespie, M. (1931). An Atropine Test in Asthma. *Brit. Med. Journ.*, Vol. II, p. 384.
- Knott, F. A., and Oriel, G. H. (1930). Detection of Histamine-like Substances in Asthmatic Sputa and Experiments on their Possible Bacteriological Origin. *Journ. Physiol.*, Vol. LXX, p. xxxi.
- Oriel, G. H. (1932). *Allergy*. London: John Bale, Sons and Danielsson, Ltd.
- Van Leeuwen, D. W. S. (1931). Clinical Treatment of Asthmatic Patients in Allergen-proof Chambers. *Journ. Lab. and Clin. Med.*, Vol. XVI, p. 442.

Medical News

AMALGAMATION OF THE ROSS INSTITUTE AND HOSPITAL FOR TROPICAL DISEASES WITH THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

We have received a memorandum by Sir C. C. MacLeod, Chairman of the Ross Institute, on the proposal to amalgamate the above institutions; this we understand has now been accepted.

This amalgamation cannot fail to be of advantage to research in tropical medicine in London, for in the first place it will mean a considerable economy in funds at a time when money is by no means plentiful and it also will mean an economy of effort because with two such institutions as the above working independently in the same locality there must have been a certain amount of overlapping. This will now be completely done away with as under the scheme of reorganization outlined in this memorandum the work of the two bodies will be altogether complementary.

The heads of departments of the Ross Institute are to be given departments in the London School and the department of tropical hygiene, which has been without a head since the death of Sir Andrew Balfour, will now be known as 'The Ross Institute of Tropical Hygiene' and it will be placed in charge of Sir Malcolm Watson.

The work that was being carried out in India under the auspices of the Ross Institute by Dr. G. C. Ramsay will be continued as heretofore.

SPECIAL COURSES IN THE STUDY OF MALARIA

We have received from the Director, League of Nations Health Organization, Eastern Bureau, notice of the first course in instruction in malaria under the direction of this body, which is to commence on 30th April, 1934, at Singapore. It is proposed to hold these courses every year and the duration of study is to be about thirty days at a cost of seventy-five Straits dollars. The laboratory and clinical course in Singapore will be followed by a month of practical training in anti-malarial work in the field in countries near Singapore where much valuable anti-malarial work is being carried on, and anti-malarial schemes on a large scale are available for demonstration.

The syllabus, of which we have received a copy, indicates that the scope of training is very wide and deals with all aspects of the problem, and if the course is carried out according to the lines laid down it cannot fail to be of the greatest value to those attending it.

Anyone requiring particulars of this course can obtain them from the Director, League of Nations Health Organization, Eastern Bureau, Singapore.

THE INTERNATIONAL ORGANIZATION OF CHEMICAL DOCUMENTATION

QUESTIONS concerning documentation have of late assumed more and more importance. Scientific and technical documents increase on all sides in such numbers that it becomes more and more difficult to gather useful material for the benefit of inquirers. There are many bodies that deal permanently with the registering, classing and diffusion of such documents. Now the co-ordination of the respective activities of these institutions on an international basis has become necessary in order to permit them to carry on their work efficiently.

As regards the province of chemistry a step was taken in 1932, in the scientific and technical sphere, by the entry into activity of the *International Office of Chemistry*, created by an international convention, and having its headquarters in Paris.

Its first act was the summoning of a conference of experts, which included the following: Messrs. *F. Donker Duvis*, Member of the Council of Patents, The Hague; *P. Dutoit*, Professor at the University of Lausanne; *P. Haber*, Director of the Kaiser-Wilhelm Institut für Physikalische Chemie und Electrochemie, Berlin; *E. Hauser*, Member of the Academy of Sciences, Madrid; *Ch. Maric*, Secretary General of the Comité International des Tables Annuelles de Constantes, Paris; *N. Parravano*, Member of the Academy of Italy, President of the Comitato Nazionale di Chimica, Rome; *G. Penny*, President of the Federation of Chemical Industries of Belgium, at Brussels; *J. C. Philip*, Professor at the Imperial College of Science and Technology, London.

The work of this conference of experts led to the adoption of a certain number of recommendations fixing the three principal tasks of the office:

I. To render accessible to all interested persons the already existing documentation, accumulated in the various centres, depots and collections.

II. To guide the chemical documentation which is in course of production, in such a way as to facilitate its registering, filing and diffusion, by methods found to be the best.

III. To ensure co-ordination between the documentation relative to chemistry and that concerning other scientific knowledge in the field of international documentation.

Thanks to these varied operations, the users of such documentation will find that all over the world a practical and rational organization of documentation in chemistry is being carried out systematically and progressively, liable to be more and more effectively adapted to their needs.

RAI SHAMBHU DAYAL SAHIB GOLD MEDAL

(1) A gold medal called the 'Rai Shambhu Dayal Sahib Gold Medal' will be presented for the best prize essay on a public health subject to be announced each year.

(2) The subject of the next essay is 'Ancient prejudices and customs which hamper public health work in these Provinces and remedies suggested to overcome them'.

(3) The competition will be open to the general public including the medical, and the public health workers, in the United Provinces.

(4) The essay is to be written in Hindi and should not exceed 3,000 words in length.

(5) Essays should reach the Medical Officer In-charge, Provincial Hygiene Institute, United Provinces, Lucknow, by 15th December, 1933.

(6) The name and address of the competitor must be distinctly written on each essay submitted and the envelope should have the words 'Prize Essay' in the top left hand corner.

(7) The Director of Public Health, United Provinces, shall judge the merit of the essay and his decision with regard to the award of the medal shall be final.

(8) No correspondence will be entered into on the subject of the competition.

(9) No essay will be returned.

BOMBAY MEDICAL COUNCIL

THE following extract from the summary of the proceedings of the meeting of the Bombay Medical Council, held on the 4th September, 1933, has been forwarded to us for publication.

The Council proceeded to consider the conduct of Mr. Motiram T. Ramchandani in giving an incorrect medical certificate against whom the Sessions Judge, Hardoi (U. P.), passed certain remarks, and as requested by the practitioner adjourned the formal inquiry into the case till February 1934.

The Council considered the case of Mr. Wazir Singh who was convicted under section 354, I. P. C., by a law court in the Punjab and directed the Registrar to erase

the name of the practitioner from the Bombay Medical Register.

The Council proceeded to consider the conduct of Mr. N. K. Panse, I.C.P.S., against whom the Assistant Sessions Judge, Sholapur, had made remarks for giving an incorrect medical certificate. After considering the reply from Mr. Panse, the Council adjourned the case till February 1934.

The Council next proceeded to consider a reference from Government forwarding the application from Mr. T. T. Shahani for permission to be registered under section 7 (3) of the Bombay Medical Act, 1922, and resolved to recommend to Government that the practitioner be given permission to be registered.

The Council considered a similar reference on an application from Mr. U. L. Bhatt and resolved that Government be informed that the practitioner may not be given permission to be registered.

The Council resolved to make a reference to Government to give certain concessions in payment of travelling allowance to members from Sind attending the Council Meetings.

The Council considered a proposal to the effect that registered medical practitioners should not associate themselves with foreign medical men who are not registered and who advertise themselves and hail their advent in lay papers, and that a registered medical practitioner should not advertise his subject and substance of lectures in lay papers, and to amend the Code of Medical Ethics to the effect that a registered practitioner should not give his or her name or surname to an institution run by him or her unless it is founded purely for charitable purpose and resolved that necessary additions and alterations be made to the Code of Ethics published for the information of registered medical practitioners.

FIFTY YEARS AGO

(From the *Indian Medical Gazette*, November, 1883, Vol. XVIII, pp. 321, 322 and 323) .

THE 'BLACK DISEASE' OF THE GARO HILLS

We are indebted to Deputy Surgeon-General J. J. Clarke, M.D., Sanitary Commissioner of Assam, for a clear though brief description of a black fever which has been known to prevail in the Garo Hills for some time past. How long it has been there it is impossible to say. Attention was first drawn to it in the year 1869, and the two features which attracted the notice of the civil officers who reported on it, were the blackness of the skin of its victims, and the great mortality caused by the disease. Numerous villages in the Garo Hills district were 'almost depopulated by the plague'. Inquiries instituted by Mr. McNaught, Civil Medical Officer of Tura, have enabled Dr. Clarke to furnish a tolerably complete account of the symptoms of the malady and to indicate the circumstances, topographical and hygienic, under which it originates and flourishes. The disease may be described as a fever resulting in a profound and fatal cachexia.

* * * * *

The disease is most intense where the low densely-wooded Garo Hills join on to the low-lying Central Assam plain, a position *par excellence* the most favourable for malarial developments. It extends also to some distance into the hill country, where the lower outer ranges are overtopped by higher interior ranges, but among these higher hills the disease is almost unknown. The villages where it is prevalent are often built in the midst of dense jungle, which the sun cannot penetrate, and where the air cannot have free access. The habitual Garo practice of annually clearing thick jungle and breaking up the ground, thus vivifying into new intensity *pro tempore* the malarious influences tends further to increase the disease. It occurs severely in the lowlands surrounding the base of the Garo Hills. This tract is only partially cultivated, swampy, totally undrained, and chiefly covered by reed or grass jungle.

We have strong support in assigning a malarial origin to this malady. The regions where it prevails could not have been better selected were malaria cultivation desired. Wells are unknown, and the water supply is mostly derived from stagnant valley water or muddy pools, which must be living masses of bacilli and infusorians adjuvant factors in the ætiology may be recognized in the facts that the habits of the Gáros are exceedingly filthy, that their food is often deficient in quantity as well as in quality, and that the poorer classes chiefly suffer. The Gáros give definite accounts of the invasion of their villages by this endemic at periods varying from 3 to 30 years previously. They firmly believe in its infectiousness, and will not communicate or associate with infected individuals. No evidence has been adduced by Europeans to prove this belief, and it is probably quite unfounded.

The question of occasional infectiousness of forms of disease usually endemic and non-infectious is an extremely difficult one, and demands inquiry of a very searching and discriminating kind. It is not uncommon for fevers of undoubtedly malarious type to assume an epidemic aspect. Such was the case with the so-called 'Burdwan fever' which caused so much sickness and mortality in Burdwan and the adjacent districts 10 years ago, and in reading of the terrible outbreaks of fever which sometimes prevail in towns and jails up-country, it is extremely difficult, apart from the question of type, to decide whether the element of contagion is or is not a factor of causation. Even as regards such a disease as pneumonia the same doubt arises, and strong reasons have been urged in favour of the view that a certain intensity of type may determine communicability.

In all cases where the area of prevalence of a disease can be defined with reasonable distinctness, and where certain conditions, topographical or hygienic, can be pointed out, as peculiar to that area, the doctrine of infectiousness must be advanced with great hesitation, and the present seems to be a case in point. A dank terrai land inhabited by a population eminently wanting in all civilized sense of comfort and cleanliness, is eminently favourable to the origin and prevalence of malarious disease, and the lesson which the interesting observations recorded by Dr. Clarke proclaim, is simply an echo of that which the history of pestilential disease has often taught, namely, that the 'black' forms of disease are due to neglect of the laws of hygiene. The suggestions, which he has formulated for the prevention of this plague, are framed in conformity with this principle, and appear to us to be thoroughly suitable and sound. They are mainly directed towards clearing and draining the sites of villages and houses, and improving the food and water of the people. These are fundamental requirements, and combined with a proper system of conservancy, we have no doubt that their realization would effect a great abatement of this *kala-azar* in respect both of prevalence and virulence.

Current Topics

A Note on Vitamins in Practical Experience

By LESLIE J. HARRIS, D.Sc., Ph.D.

(From the *British Medical Journal*, 5th August, 1933, p. 231)

IN my paper to the Section of Diseases of Children at the Dublin Meeting of the British Medical Association, dealing with the practical significance of vitamins in day to day clinical experience, I have confined my attention largely to the anti-rickets vitamin D, which, of course, in this country, is the factor of pre-eminent importance. A list of conclusions is, however, included relating to vitamins A, B, and C and certain other

practical issues; and it is the purpose of the present brief notes to summarize the evidence on which these conclusions are based.

VITAMIN A NOT A GENERAL ANTI-INFECTION AGENT

Week by week advertisers' announcements are sent to us all by post, or appear in the journals, which rather convey the impression that vitamin A builds up the general resistance to infection and is of value in the treatment of toxemias and infectious diseases of all kinds. This is claiming far too much. Vitamin A is anti-infective in only a limited way. As I have shown, in collaboration with J. R. M. Innes, the local infections to which vitamin A deficiency gives rise are of a quite special type, being caused by structural breakdown of membranes. There is no change in the general immunity. These scattered, localized infections are restricted in origin to the abnormal membrane, and are set up by chance micro-organisms which would normally prove to be non-pathogenic. There is no reason to suppose that vitamin A could exert any direct bactericidal or similar effect when given in definite cases of infectious diseases and septicaemias caused by the invasion of specific virulent micro-organisms. Dr. Griffith and I showed, for example, that vitamin A had no effect on the spread of experimental tuberculous disease. Again, our colleague Dr. Thomas Moore has found that in human beings dead from the most varied types of infectious diseases there may be abundant reserves of vitamin A in the body, so that little could have been gained by its administration in such cases, and it is obviously no longer possible to regard the vitamin as an anti-infective agent indiscriminate in its scope. The original observation which held out the hope of wide positive therapeutic uses for vitamin A was that of Mellanby and Green; it appeared to show that in puerperal septicemia the mortality was strikingly diminished as a result of vitamin A treatment. Mellanby suggested that many common infective conditions might be due to vitamin A deficiency, including the common cold, acute rheumatism, phthisis, bronchitis, pneumonia, middle-ear disease, ulcerations of mouth and eyes, and inflammations of nasal sinuses. However, later clinical investigations by many workers have shown that vitamin A therapy has failed to have any effect as a prophylactic in respiratory diseases, in the common cold in infants, on the incidence of common infections generally, or in the treatment of pneumonia. As has been agreed by Mellanby, a difficulty in interpreting his original, apparently favourable, results in puerperal septicemia is the great natural variation in virulence from case to case. Ellison claims to have reduced the mortality rate in measles in young children by treatment with vitamins A and D. In a group of 300 cases so treated there were eleven deaths, and in a similar control group of 300 given no extra vitamins twenty-six deaths. Further statistical evidence will, of course, be needed before the claim can be regarded as definitely established. Ellison points out how there often occurs after severe measles a metaplasia in the respiratory tract resembling that of vitamin A deficiency, and this might be regarded as providing a rationale for the treatment. We may certainly admit that it is in young children—the class studied by Ellison—that any liability to shortage of vitamin A seems most likely to occur (see below).

VITAMIN A REQUIREMENTS

Although we are satisfied that vitamin A is of no value as a general anti-infective agent for indiscriminate use in treating all kinds of infectious diseases it is still important to ensure that enough of the vitamin is given in the diet, as there is full evidence to show that a lack must lead to specific ill effects (including xerophthalmia, or night-blindness, often accompanied by tendency to respiratory infection. In many parts of the world avitaminosis A is widespread, while it will come as a surprise to most to hear that in this country it is not quite unknown, no fewer than seventeen cases

of xerophthalmia being recorded in one year in a North of England hospital. A recent report from America gives details of thirteen such cases in under-nourished children. As to the more difficult question of partial lack of this vitamin (hypovitaminosis) it is hard to speak with any certainty. The results of Moore for the British Isles and of Wolff for the Netherlands suggest that about 16 per cent of the population might perhaps be considered to have 'sub-normal' reserves, but it is difficult to know how to fix the limit for normality. The reserves found vary immensely from one individual to another.

Work by my colleague Dr. W. J. Dann, in particular, has shown that the young of the species receive a surprisingly limited amount of vitamin A *in utero* and in their mother's milk, so that the need for ample provision of this factor *especially at weaning* becomes all the more apparent. Vitamin A is found in most animal fats (except lard) and fish oils; but carotene, which is of equal biological value and is converted to vitamin A by the animal (as shown by Moore at Cambridge), is as readily accessible in green vegetables, carrots, etc. We may sum up the matter of vitamin A dosage by drawing a contrast between it and its fat-soluble companion D. Whereas with vitamin D no common food-stuff contains an abundance, so that supplementary dosing is an absolute essential if the deficiency (rickets) is to be averted, many common articles (any common greenstuffs) contain all that is needed of vitamin A, so that separate dosing cannot be regarded as being so imperative, but merely as an additional safeguard in cases of doubt.

VITAMINS B₁ AND B₂

Vitamin B₁ deficiency (beri-beri), including the infantile variety, is almost universal in certain parts of the globe, but there is little evidence of any serious lack of this vitamin in this country or in the U. S. A. True, the possibility of some partial want is suggested by experiments recently carried out in America, which showed apparently quite conclusively that when sources of extra vitamin B were added to the diet of large groups of infants the growth rate or weight curves, or both, were far ahead of those of the control groups. We must await further tests before dogmatic statements can be justified. Intestinal stasis and lack of alimentary tone is admittedly one effect of vitamin B deficiency, but in my opinion there is no compelling evidence for the widely advocated theory that the prevalence of constipation in this country is due to vitamin B shortage. Pellagra (vitamin B₂ deficiency) has an astonishingly high incidence in the U. S. A. (170,000 cases in 1917; 120,000 cases in 1927; mortality rate about 40 per cent), but it is not a disease of children, and is therefore outside the scope of our present discussion.

VITAMIN C

It is nowadays the recognized orthodox practice to give all bottle-fed infants fruit juice for the purpose of preventing Barlow's disease (infantile scurvy—that is, deficiency of vitamin C, recently identified with *hexuronic* or '*ascorbic*' acid). This is an essential procedure, as cow's milk is a rather poor source of vitamin C, and pasteurization may destroy what little there is—this, to a greater or less extent depends on the conditions of the pasteurization, the presence of copper particularly inactivating the vitamin. This question is of much current interest and importance in view of the proposed legalization of compulsory pasteurization—a process which, it may be noted in parenthesis, is of commercial benefit to the dairying interests, since pasteurized milk 'keeps' longer and can be sold when staler. We do not know at all accurately to what extent vitamin C underfeeding is current in this country; but the fact that definite outbreaks of scurvy tend to appear (as in Manchester, Glasgow, and Newcastle in 1917) whenever there is a failure in the potato crop suggests that many people must be near the borderline, and that they rely too exclusively on

the potato as their sole source of the vitamin. The consumption of other vegetables and salads and fruit should be encouraged: a useful 'rule' that has been advocated is to spend as much on fruit and vegetables as you do on meats and fish and, incidentally, the same sum again on *milk*. (Here, of course, we are speaking of children and adults, not young infants.) In Sweden Göthlin believes, from his tests on capillary strength, as measured by the liability to cutaneous hæmorrhage under given pressures applied to the skin, that 18 per cent of a group of country school children were suffering from hypovitaminosis C. E. W. Fish and I find that vitamin C deficiency in experimental animals leads not only to failure in function of odontoblasts (as had been previously observed), but also to faults in enamel formation of the type which precedes dental caries in man. It is quite likely that deficiency of vitamin C—no less than of vitamin D, which has been studied so fully by M. Mellanby—may often be a contributing cause of dental caries.

OTHER NUTRITIONAL FACTORS

I would not wish to close without making at least a cursory allusion to nutritional factors other than vitamins, lest I might seem to convey the impression that vitamins alone mattered. Among the most striking of recent work is that of Mackay, who has shown how surprisingly common is iron deficiency in infants, and has published a convincing account of the beneficial effects of its administration in such cases. The observations, too, of Corry Mann on the unique nutritional properties of milk for school children, work which has since been amply confirmed up and down the country, call for special mention.

THEORY AND PRACTICE

In conclusion, we must realize that our problem cannot be divorced from economic realities. Calculation shows that the cheapest diet for bare sustenance costs about 5s. to 7s. a week for an adult, or about 3s. to 4s. for a child. This figure assumes a knowledge of how to choose food to the best physiological advantage, and also the opportunity of purchasing it in the cheapest markets. Yet it has been shown that even this minimal sum is beyond the reach of many of the unemployed, whose income falls short of that amount after deducting only for rent, and making no provision whatsoever for such necessities as clothes, heating, etc. The fault here lies not with science, but largely in the malorganization of society, and sometimes too in a failure to apply or to realize the knowledge which science has already won. In America it has been found worth while to employ whole corps of 'nutritionists', whose function is to advise the public authorities as to nutritional conditions and local needs, and to instruct households on the outlay of their budgets.

Remarks on Essential Vascular Hypertension

By SIR HUMPHRY ROLLESTON, *Bart., A.C.N.O., R.C.B., M.D.*

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NATURE OF ESSENTIAL HYPERTENSION

ESSENTIAL HYPERTENSION may be briefly described as a persistently raised systolic and diastolic blood pressure not due to arterio-capillary, renal, cerebral, or other recognizable morbid change. It therefore resembles chronic splenic anaemia, in that many cases of undetermined aetiology are grouped under one descriptive term. It may however, cause, and be the antecedent stage of, cardiovascular changes, renal fibrosis, and their various results. There is good evidence that a raised blood pressure and renal disease can each cause the other, and that, in an early stage, the renal lesion wrought by hypertension is an arteriolar thickening and narrowing in an otherwise normal organ.

It has often been urged that high blood pressure is a compensatory adaptation to maintain an efficient circulation through the kidneys, brain and myocardium. Reid's observations on patients did not support this view as regards renal function. Experimentally increase of the intracranial pressure above that in the cerebral arteries produces anaemia of the brain, and thus calls forth, through the vasomotor centre, a general rise of the systemic arterial blood pressure. Starling suggested arteriolar proliferation in the vasomotor centre as the cause of hypertension. Bordley and Baker found a definite association between hypertension and arteriosclerosis in the medulla oblongata; out of twenty-four cases of generalized arteriosclerosis, fourteen with constantly raised blood pressure showed arteriolar changes in the medulla, whereas in the remaining ten cases with normal blood pressure the medulla was free from arteriolar changes. Cutler nor Tuthill could confirm this correlation. According to Evans, hypertension and the diffuse hyperplastic sclerosis of the arterioles are concomitant effects of the same cause. MacWilliam, after a full physiological discussion, concluded that the hypertensive impulse, however caused, emanates from the controlling vasomotor centre in the medulla. It has been suggested that the condition may depend on hypersensitiveness of the vasomotor centre, but as the result of experiments Kroetz contested this. Vasomotor instability is present in many cases of hypertension, but whether as the primary cause, as a concomitant reaction, or as a result is open to debate. It is conceivable that a metabolic poison selectively constricts the arterioles of the vasomotor centre, and that the resulting ischaemia stimulates pressor impulses.

That the peripheral obstruction responsible for high blood pressure is due to spasm and not to structural narrowing was rendered highly probable more than forty years ago by W. H. Broadbent's observation that vasodilators such as amyl nitrite produce a fall of pressure. Clinical observation proves that arteriosclerosis and high blood pressure, though often associated, occur independently of each other; there is indeed much more evidence that long-continued hypertension is responsible for degenerative arterial changes than that ordinary arteriosclerosis raises the blood pressure. The site of the peripheral obstruction in essential hypertension, whether in the arterioles, as is suggested by their visible constriction in the retina, in the capillaries, or in both, is an open question, and it is quite conceivable that it varies.

The constant normal fluctuations in the capillary bed, however, render it doubtful if the capillary pressure estimated in the skin represents that in the extensive splanchnic and other deep areas of the body. Kylin stated that the capillary pressure is raised in glomerulonephritis, in which there is widespread capillary change, but is normal in essential hypertension; Boas and Mufson, however, found the capillary pressure high in seventeen and normal or low in twenty-eight out of forty-five cases of essential hypertension.

A division has been made into benign and malignant hypertension. But the malignant form is apparently a complication with diffuse change in the arterioles, which in some rare recorded cases has resembled that in periarteritis nodosa. It mainly occurs in the comparatively young, in the fourth decade, and runs a rapid course with very high blood pressure, acute functional failure of the brain, myocardium, and kidneys, death being often due to uræmia. Fahr described the renal changes as malignant nephrosclerosis, and Boyd as resembling those in the 'flea-bitten' kidney due to the embolic focal glomerulo-nephritis in subacute bacterial endocarditis with necrotic changes due to ischaemia. It is therefore clear that 'malignant hypertension' differs from uncomplicated essential hypertension.

ÆTIOLOGY

If it be accepted that essential hypertension proceeds, and may eventually be responsible for, arteriosclerosis and chronic renal sclerosis and not vice versa,

what are its causes? A persistently raised blood pressure is a retention, and it is no longer necessary, in obedience to the law that there is 'but one cause for one effect', to explain all cases of essential hypertension by a single and therefore specific factor such as renal inadequacy, endocrine disorders, mental worry, or errors of metabolism. While it is safest to take an agnostic attitude about the cause, many hypotheses have been put forward.

Heredity.—Heredity has been rightly considered to be a disposing factor. It is shown to be so by family records, from a study of which Weitz concluded that 'genuine or vascular' hypertension is a constitutional disease with dominant Mendelian characters. George Draper has tabulated the anthropometric characters of those prone to become the subjects of hypertension, and Major recently illustrated the influence of heredity by the freedom from high blood pressure of the pure-bred Chinese, with their Oriental calm, in the past. In the symposium, *Arteriosclerosis* (1933), edited by Cowdry, both Lange and G. D. Williams throw doubt on the influence of heredity in the majority of cases.

Endocrine disorders

In addition to the nervous mechanism of the sympathetic and parasympathetic, chemical factors play an important part in the control of the circulation, the two mechanisms being closely related. The chemical messengers or hormones exerting a pressor effect are adrenaline and vasopressin (posterior lobe of the pituitary).

An excessive secretion of adrenaline (hyper-nephrism) was suggested as a cause of hypertension in 1904 by Vaquez, Josué, and others; but, as evidence of adrenal overactivity, stress was laid on hyperplasia of the cortex, which may well have been a secondary lipid storage, and as numerous observers failed to find a greater pressor effect from the blood of hypertensive than from the blood of normal subjects, the view failed to carry conviction. It has been revived, however, by Vaquez, with very definite reference to overactivity of the chromaffin system, by Paul, and by Goldzieher who has described hyperplasia of the adrenal medulla. So far, however, the presence of adrenaline in the blood of subjects with essential hypertension has not been established.

Primary adrenal tumours have, in rather exceptional instances, been associated with hypertension, and a brief reference to this subject has some bearing on the hypothesis that hyper-adrenæmia is responsible for essential hypertension. Of the various forms of primary adrenal tumours some, especially the undifferentiated tumours (neuroblastomas) of the medulla, are not associated with a raised pressure, whereas the subjects of well-differentiated chromaffin tumours may experience paroxysmal crises of high blood pressure, a condition distinct from essential hypertension. Some cortical tumours, contrary to what would logically be anticipated, have been associated with persistently raised blood pressure.

Primary tumours of mature chromaffin cells (phaeochromocytomas when arising from the adrenal medulla, paragangliomas when derived from chromaffin cells elsewhere) are rare; Rabin collected thirty cases, in ten of which the blood pressure was raised. Marcel Labbé recorded a case with paroxysmal hypertension, and later collected eight of a similar character. Adrenaline has been found in these tumours. These crises, between which the blood pressure may be normal, follow slight exertion, or occur without obvious cause; the blood pressure may rise to 300 mm. Hg., and pulmonary oedema may occur. They may perhaps be regarded as the pathological equivalent of the events described in Cannon's 'emergency hypothesis'—namely, discharge into the circulation of adrenaline in excessive amounts in response to emotions such as fear. This form of paroxysmal arterial hypertension varies much in degree and duration, the latter from seconds to days (Castex). The attacks have been regarded as much

the same as those of Nothnagel's angina pectoris vasomotoria and those due to intravenous injection of adrenaline. Freedom from further crises has followed removal of the tumour.

Primary tumours of the cortex have been associated with a continuously raised blood pressure in rather exceptional cases, which have been recorded and collected by Volhard, Langeron, and Lohéac. The cortical tumours may be bilateral. It is not known if these cortical tumours are constantly derived from any one of the usually described three zones of the cortex. Cushing, however, brought forward evidence that some at least of the reported cases of cortico-adrenal hypertension are examples of basophil adenoma of the anterior lobe of the pituitary.

Deficiency of hypotensive bodies in the circulation is, as pointed out by MacWilliam, a possible cause of hypertension. The extracts of many organs and tissues—some, such as histamine, choline, acetylcholine, and adenosine, known, others, from the liver and brain, unidentified—exert a depressor influence on blood pressure. But apart from these reference may be made to the hormone vagotonine, recently isolated from the pancreas by Santenise; it is separable from insulin, increases the reflex excitability of the vagus and parasympathetic, and exerts a depressor influence different from that of choline, histamine, adenosine, peptone, and from the other hypotensive bodies extracted from the pancreas by Livon, P. Gley and Kistlinios, and Frey and Krant ('kallikrein'). Whereas the latter extracts produce an immediate fall of blood pressure which may be followed by a rise, the hypotensive effect of intravenous or hypodermic injection of vagotonine is delayed, slowly progressive, prolonged, and never followed by a hypertensive reaction. An intravenous injection of vagotonine before one of adrenaline inhibits the secretion and impairs the activity rather than directly neutralizes the action of adrenaline.

That vagotonine may play a part in controlling the rise of blood pressure and its absence in some cases account for hypertension is perhaps supported by the observation that in uncomplicated hypertension the tonus of the sympathetic nervous system was increased and that of the parasympathetic diminished, as compared with normal subjects; and also by the frequency of a low sugar-tolerance in hypertensive subjects, for Santenise found that vagotonine has a hypoglycæmic effect less rapid in onset, but more prolonged, than that of insulin. Abrami, Santenise, and Bernal have treated eighty patients with high blood pressure of various kinds by vagotonine, usually by hypodermic injection: thirty of these were permanently better after a series of injections, the best results being obtained in those with paroxysmal crises of hypertension: a number of patients did not respond to vagotonine. These results, taken in conjunction with the paroxysmal crises of high blood pressure in patients with chromaffin-celled tumours of the adrenals, lend support to the view that essential hypertension is not due to excess of adrenaline in the blood. An unidentified depressor substance present in the urine of normal persons has been found to be absent from the urine of hypertensive patients by Wollheim and Lange.

The hypertension about the time of the menopause, often in fat women and coincident with arthritis, has been ascribed to, as it is contemporaneous with, endocrine changes. The evidence is at the best circumstantial. Ayman and Pratt consider that the hypertension is psychical in origin; this explanation is on the same lines as Kylin's view, that hypertension is a manifestation of a general nervous disorder, especially of the automatic system. But this only shifts back the question of causation.

Pressor substances.—Many investigations have been undertaken to isolate pressor substances, other than adrenaline, in the blood, and due to disturbed metabolism or to imperfect excretion, especially of protein derivatives. Persistent, and at the same time cautious, claims have been made since 1924 by Major on behalf

of guanidine bases; in approximately 50 per cent of a large number of hypertensive subjects he has obtained evidence of an increase in the blood of a substance with reactions resembling those of guanidine; this has been confirmed by Pfiffner and Myers. Major has also observed a fall of blood pressure in hypertensive patients when induced diuresis caused an increased output of this substance in the urine. Waldbott's conclusion that some cases of unexplained hypertension may be caused by allergy was tested and contested by Cohen, Fineberg, and Rudolph. 'A distinct therapeutic success' in reducing hypertension was reported by Allen and Sherrill by restriction of the sodium chloride intake; but this was contested by Mosenthal and by Berger and Fineberg.

Psychical influences.—In 1876, at the Sheffield Meeting of the British Medical Association, Clifford Allbutt read a paper on 'Mental Anxiety as a Cause of Granular Kidney'. As acute emotion causes a temporary rise of blood pressure it has been assumed that long-continued worry, or the strain of strenuous existence, may be responsible for essential hypertension; but it must be remembered that mental strain is often accompanied by circumstances harmful to health, such as overeating and want of fresh air and of exercise. Some doubt has been thrown on this influence of mental strain by Soma Weiss's analysis of 33,000 life assurance applicants with a systolic pressure of 170 and a diastolic of 100 mm. Hg.; this showed that the average blood pressure of small farmers was as high as, or slightly higher than, that of lawyers, medical men, teachers, and members of other professions specially exposed to mental strain. Long-continued mental strain and worry are very common, and no doubt many with this history become hypertensive; but many escape and by no means all hypertensive patients have led a strenuous life. That mental worry may have some influence, especially in those with an hereditary tendency and when combined with other unfavourable circumstances, cannot be denied; but as a single efficient cause its claim must not be rated too high.

CLINICAL SIGNIFICANCE

Lastly, a few words on the clinical significance. Although symptoms may occur in patients with essential hypertension, what evidence is there that they are due solely to the persistently raised blood pressure rather than to its cause or to the effects of its long-continued action on the cardiovascular system or kidneys? It is common knowledge that hypertension may exist in persons who do not complain of any symptoms, at any rate until they learn, perhaps after an examination for life assurance, that their blood pressure is too high. The subjects of uncomplicated hypertension are prone to vasomotor instability, and hence fluctuations in the blood pressure occur more readily than in normal persons. These subjects may be free from symptoms while the raised blood pressure remains fixed at the level best suited to the individual, and so long as secondary changes, such as cardiac and renal failure, are absent. But a sudden considerable rise may precipitate discomfort just as in paroxysmal hypertension. It has been thought that the early symptoms of essential hypertension are due to functional disturbances of the blood supply of the brain, either by spasm or by causing increased intracranial pressure of the cerebro-spinal fluid.

Polycythaemia.—The red count may be increased in hypertension; in some degree it was present in 45 per cent of Kerppola's cases, and Lenaz found a definite relation between the systolic blood pressure and the red count, systolic pressures of 125, 150, and 170 being associated with 5, 6, and 6.8 million red cells per c.mm. Attempts to explain this occasional association are not very convincing. In polycythaemia rubra or erythraemia the viscosity of the blood is increased, and in Gaisböck's group of polycythaemia hypotonica the blood pressure is raised, but these cases are usually complicated by

chronic nephritis. Among 189 collected cases of polycythaemia Lucas found records of the blood pressure in sixty-six, and in twenty-one, or one-third, of these, the systolic blood pressure was below 140; this suggests that neither polycythaemia nor the constant viscosity of blood is responsible for the raised blood pressure. It has, however, been argued that polycythaemia is not due to arterial hypertension alone, but to raised pressure in the capillaries, which leads to concentration and a fall in the water content of the blood. The divergence of opinion, however, about the capillary pressure in hypertension renders further investigation and information necessary before this correlation can be considered. Izquierdo and Cannon's discussion of 'emotional' polycythaemia in relation to the sympathetic and the medullary-adrenal action of the spleen, and Lamson's earlier view that excess of adrenaline in the blood may drive the red cells out of the spleen into the circulation, might suggest that those cases of essential hypertension with polycythaemia have an excess of adrenaline in the blood. The simplest explanation of the association of polycythaemia and essential hypertension is the onset of congestive heart failure.

In conclusion, the clinical significance of essential hypertension is obviously that it is the potential antecedent of cardiovascular and renal complications.

Entamoeba histolytica Carriers and Their Treatment

By LIEUT.-COL. H. W. ACTON, C.I.E., I.M.S.

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INTRODUCTION

Erroneous ideas still exist as to the exact rôle played by *Entamoeba histolytica* in producing the various clinical symptoms associated with its presence in man. At first the term 'amoebic dysentery' was used synonymously with 'amoebic colitis' so that the clinical syndrome, and dysentery, i.e., the passage of frequent stools containing blood, pus and mucus, accompanied with tenesmus, was looked upon as a necessary concomitant of this infection. In ordinary civil practice this, however, is not the case as acute amoebic dysentery is a fairly rare complication of amoebic colitis—I should not place it higher than 5 per cent in an ordinary well-fed population. The incidence rises very much higher, 25 per cent or more, in the debilitated where the condition is brought about by malnutrition (famine and war) or as the result of chronic diseases such as chronic malaria, kala-azar or bacillary dysentery. The extensive ulceration of the bowel seen in some of the more severe cases of acute amoebic dysentery is due to the breaking down of the local tissue defences (kataphylaxia) as the result of a vitamin deficiency. This tissue in turn may be secondarily infected with the development of hospital phagedena, etc. The picture is seen under exceptional conditions such as war, famine, maladministration. In actual practice, however, the lesions in the bowel are usually so trivial and so slight as, at first, to interfere only with the proper movement of the gut, and give rise to constipation. I generally teach that the commonest symptom of amoebic colitis is not dysentery but constipation and that some patients have to take a daily dose of saline to prevent it.

In patients in whom it is difficult to relieve the constipation, stasis of the caecum may occur with an extension of the ulcerated surfaces. In such persons the constipation may alternate with diarrhoea due to the stasis, or there may be a morning irritative diarrhoea as the result of irritation by alcohol, foods or chill, the stools containing a good deal of mucus. This is the common type of *E. histolytica* carrier seen in practice. One must also clearly recognize that this amoeba can live a purely coprozoic life in the large bowel without producing any lesions of the mucosa or symptoms in

the patient. Dobell has shown that, in the common monkey *Macaca irus*, *E. histolytica* lives a purely coprozoic life. I have seen two such cases in man in whom numerous *E. histolytica* were found during the course of routine microscopical examinations, while at post-mortem examination two days later no visible lesions were observed in the mucosa of the large intestine. Such cases can also be recognized after careful clinical and pathological examinations. These are the true coprozoic carriers of *E. histolytica* who have no symptoms and are without ulcerative lesions in the gut. During the war I saw a unique case of this type. The patient was passing liquid watery stools containing numerous adult *E. histolytica*. There were no blood or pus cells seen and bacteriologically vibrios were not found. The patient died of broncho-pneumonia 48 hours later, and at the post-mortem examination no lesions were seen in the bowel.

The next point to determine is the factor or factors that allow *E. histolytica* to penetrate the healthy mucous membrane and gain the submucous layer. A study of the early lesions shows that over a small area of the surface epithelium of the gut there has been a breach in the surface, exposing the submucosa to the contents of the lumen of the gut. The amœba can now make its way into the tissues, and wander some considerable distance from the point of entry. Those deep down in the tissues do not contain red blood cells but often lie in little pools of lysed tissue. The adult amœba near the surface contain red blood cells and encystation occurs when the amœbæ are exposed to the contents of the gut at the surface of the ulcers. The method of entry is through some superficial trauma, and in the tropics there is ample opportunity for loss of surface epithelium as a result of injury from helminths, *Trichuris* and *Enterobius*, and from the ulcerations produced in the different types of bacillary colitis. We are not surprised to find that 15 per cent of our cases carrying *E. histolytica* have also bacilli of the dysentery group present in the stools. We have thus the mixed carrier of bacillary and amœbic infection to deal with.

The second factor that helps to keep up the carrier state is stasis. Sellard has shown that a condition of stasis of the bowel is essential before experimental infection can occur in animals. In man there is no doubt that the constipation and irregularity of the bowel that is so constantly present is responsible for the occurrence of stasis. Many of these cases find, from practical experience, that if the bowels are kept open daily with salines they are free from any symptoms. As the stasis increases the faecal contents remain in the cæcum longer and longer, so that (1) the time interval being lengthened there is opportunity for excystation of the amœbæ in the gut and increase or persistence of the carrier state; (2) the decomposition products irritate the cells of the mucous membrane of the cæcum so that an excess of mucus is poured out, hence the significance of the presence of mucus in the stools; (3) the character of the bacterial flora in the stool becomes profoundly altered. The greatest change is in the number of fine streptococcal colonies seen on the Conradi glucose plates, causing sometimes a haze on top of the medium. These are replacing the larger coliform organisms. Usually it may be stated that the more numerous the number of these colonies the more extensive is the ulceration in the gut. When there is much fermentation going on in the cæcum and large intestine the more numerous are the large moist colonies of bacteria of the ærogenes group. In the mixed type of bacillary and amœbic carrier, a varying number of opaque non-lactose-fermenting colonies may be seen which may be identified as atypical dysentery bacilli or *Bacillus pseudo-carolinus* and *B. morganii* or late lactose fermenters, as those of the metadysentery group.

The effect of stasis varies with the individual.

(1) The absorption of food may be impaired. Some of these carriers are always thin and sallow, whilst others may put on weight and remain stout.

(2) Certain hormones may be stimulated or depressed resulting commonly, in the Indian, in leucoderma and hyperadrenia, and, in the elderly European, in hypoglycæmia.

(3) Allergic phenomena from the abnormal decomposition of common food-stuffs, such as eggs, chicken, milk, flour, potatoes, may occur, and give rise to urticaria of various kinds, pityriasis rubra, toxic erythemas including erythema multiforme and asthma.

Types of *E. histolytica* carriers

Our analysis shows that there are three different and definite types of *E. histolytica* carriers, namely:—

I. Coprozoic carriers who have no lesions and no symptoms.

II. Pathogenic carriers with lesions and slight symptoms.

III. Carriers which have also bacilli of the dysentery group (mixed carriers).

The total number of these carriers amongst a given population varies. In Calcutta the percentage is between 10 and 15 per cent; in Mesopotamia, amongst the personnel who had been two years in the country, it was over 20 per cent. The figure quoted for England is between 3 and 5 per cent, as stated by Dobell. In India and the tropics the lesion in the pathogenic carrier is the commonest source of septic foci in the body. In England, as far as I can make out, practically no attention is paid to this. The reason may be due to the fact that the majority of carriers seen in the temperate zone are not pathogenic but coprozoic carriers and hence do not exhibit septic foci.

The high percentage of mixed carriers, i.e., 15 per cent amongst the Calcutta population, is important from two points of view. Firstly it shows that there is a partial correlation between the two types of dysentery organisms, and secondly it accounts for the difficulty of curing such cases by emetine only. In India there are two types of carriers who come to me for treatment; those who have failed to be cured by emetine, emetine bismuth iodide or other variations of it, and those who have symptoms not suspected to be due to the intestinal condition, such as myocarditis, hypoglycæmia, leucoderma, filarial fever.

The procedure adopted in hospital for the diagnosis of these cases is:—

(1) A specimen of the stool, preferably the last specimen passed, is sent to the laboratory daily for five days, or until a positive finding is obtained.

(2) The first stool passed in the morning is plated by a technician, immediately after being passed, on 1 per cent bile salt, McConkey's media and Conradi's litmus glucose agar. Sabouraud's medium for *Monilia* and Norris's synthetic medium for special cases are also used when the physician considers it necessary.

When there is evidence of bacterial emboli, 50 c.c. to 100 c.c. of urine is taken off and placed for 12 hours in the incubator, the urine itself being an excellent culture medium. If it becomes turbid, it is replated on McConkey's medium or Conradi's glucose agar.

Formerly, when allergic phenomena were present, we carried out the various food tests but with experience we abandoned them, as they never gave any information other than that the patient was sensitive to half a dozen, or all the foods tested. If alteration in the function of the different endocrine glands is suspected we do the ordinary standard tests: blood sugar, Gotch's test, basal metabolism.

THE *E. histolytica* CARRIERS FROM A CLINICAL AND DIAGNOSTIC POINT OF VIEW

(I) *Coprozoic carriers*.—These are fairly rare in the tropics as, sooner or later, they almost certainly pass into the next class. Such coprozoic carriers should pass normal stools without mucus; the temperature should be normal and there should be no history of symptoms of emboli, allergy or endocrine defects. Microscopically there are numerous *E. histolytica* cysts, often associated with the cysts of *Chilomastix mesnili*, *Iodamoeba*

butschlii and *Endolimax nana*. As a rule no Charcot-Leyden crystals or pyknotic cells are seen. The plating results show the flora to consist of chiefly lactose-fermenting colonies, and a very few small colonies which are usually fine yeasts and not streptococci.

(II) *Pathogenic carriers*.—These are the important cases, as from time to time they exhibit symptoms and signs of the disease in the bowel or in other parts of the body.

From a general point of view, such pathogenic carriers may appear perfectly healthy, but on questioning, a tendency towards constipation may be revealed, which has to be corrected by a morning saline; from time to time mucus may be seen in the stools. On the other hand some individuals are thin and do not lose or gain weight in spite of what they eat; the complexion may be muddy, the tongue furred, and the bowels irregular with the passage of mucus. The night sleep does not freshen up these patients who are tired out by the end of the day. These cases, unless diagnosed in time, may develop neurasthenia. More commonly there are long latent periods when symptoms are absent, unless the lesions are irritated by chills or errors of diet. In the old days the use of the flannel belt was a very good indication of the existence of the amœbic carrier state, but now, with the wholesale use of emetine in any bowel affection, the cholera belt is rapidly disappearing.

The first group of symptoms seen in these cases is due to kataphylaxia, i.e., a breaking down of the local defence mechanism in the floor of the ulcer, giving rise to emboli of cocci in the blood stream. Before these symptoms appear, the patient often complains of an increase in mucus in the stool, diarrhoea, and other intestinal symptoms.

Hæmolytic streptococci can be isolated from the stools and very often from the urine, during an attack. Sometimes, however, *Staphylococcus mollis* is found instead of streptococci. The bacterial emboli may lodge in the vessels of the nerves, causing sciatica, brachial neuritis; in the muscles, producing myositis and lumbago; in the vicinity of joints, giving rise to synovitis, arthritis and lesions in ligaments about the vertebral column. After the age of 45 these septic foci in the gut fairly frequently cause myocarditis. In filariasis they often produce bacterial inflammatory lesions round the dead or dying worms, conditions seen clinically as endemic funiculitis, filarial colic, abscess of the cord, orchitis, filarial abscess and acute filarial cellulitis. Lately Colonel R. B. Lloyd has been able to differentiate these septic cases from the cases produced by filarial toxins. In the septic cases there is leucocytosis; and the complement test against *Dirofilaria immitis* antigen is not altered or is negative. The amœbæ themselves may also leave the bowel, owing to congestion, and be caught up in the fine capillaries of the liver, causing amœbic hepatitis. I am extremely doubtful whether large adult amœbæ can ever pass through the fine filtering capillaries of the liver and invade other organs of the body. I have seen two cases of cerebral abscess secondary to extensive amœbic ulceration of the gut and from both abscesses an *Actinomyces*, probably *asteroides*, was recovered.

The second group of symptoms produced in these pathogenic carriers is due to stasis, the effects of which, on the general metabolism, should first be considered. Some carriers seem to thrive in spite of these changes, whilst others gradually become thin and pass into a neurasthenic condition. The thyroid and adrenals show evidence of loss of function—harsh skin, a feeling of cold, low blood pressure. We have seen two other endocrine defects that are correlated partially with the carrier condition. The one is leucoderma, associated with hyperadrenia in Indians; and the other, hypoglycæmia in elderly Europeans, which is the converse of diabetes, in the Indian at the same age. When there is a good deal of decomposition proceeding in the gut, the proteins of the commoner foods, chicken, eggs, milk, potato and bread, are split up probably into abnormal

end-products so that these patients now become sensitive to these common foods. This type of allergy is very commonly present in the case of urticaria of adults, eczema rubra of children, in pityriasis rubra and, more rarely, the acquired asthma of adults.

The lesions of the symptomatic or pathogenic *E. histolytica* carrier are the great source of septic foci in the gut and a cause of acquired allergy from the gut.

Bacteriological examination.—The consistency of the stool is variable in these cases. It may be constipated, with small patches of mucus, or loose with mucus and unusually offensive. Microscopically there can be detected mucus, frequently pyknotic cells and sometimes Charcot-Leyden crystals. The last named are probably some simple protein like spermin, and represent an end-product of protein decomposition: I took upon them as an evidence of stasis. I have seen the *E. histolytica* ingesting these Charcot-Leyden crystals on the floor of an amœbic ulcer, prior to encystment. The number of amœbæ in the stool is variable. They may be few or numerous, while 'minuta' forms as well as cysts may be seen. Other protozoa like *Endolimax nana* and *Iodamoeba butschlii* may be present in both cystic and vegetative forms. Bacteriological cultures on glucose Conradi plates reveal many fine streptococcal colonies, which are characteristic of the pathogenic carrier: the more acute the lesion the more numerous the streptococcal colonies. On McConkey's plates the lactose-fermenting colonies of the coliform type become fewer and fewer in number and when there is a good deal of gas-forming decomposition with stasis, numerous larger, paler and moist colonies of the *lactis aerogenes* type are seen.

(III) *Mixed carriers of amœbic and bacillary infection*.—About 15 per cent of the amœbic carriers seen at the School of Tropical Medicine in Calcutta have both infections. This point is of some practical importance as the difficulty of curing them by emetine or even emetine bismuth iodide is the cause of their being sent to us. These chronic mixed carriers differ considerably in their symptoms from the pure amœbic carriers. Reflex spasms are more common at the pylorus, upper part of cæcum, transverse and descending colon. Many of these cases have had the appendix removed and still have tenderness in this region. A few develop signs of duodenitis and even gastric or duodenal ulcer. The Gram-negative bacilli that leave these ulcers do not cause emboli. They are commonly excreted in the bile or urine and may give rise, rarely, to attacks of continued fever (e.g., *B. asiaticus*). In the urinary tract they may cause cystitis, when a cystocele is present or pyelitis, from the pressure of a pregnant uterus. Bacteriologically on the McConkey plates, in addition, one will see a few or a number of opaque non-lactose fermenters, or late lactose fermenters.

TREATMENT

The routine treatment adopted for these cases was the administration of bismuth emetine iodide as advocated by Dobell, with slight modifications. Two grains of bismuth emetine iodide powder were given at night in liquid paraffin (one drachm), as it had been found in military practice that the use of tablets was followed by their being found on the ground, unswallowed, next morning, while in the tropics they may also pass unchanged through the bowel. An hour before this dose one-sixth grain of omnopon (Roche) was given and when the patient had become drowsy the bismuth emetine iodide was administered. The course of treatment lasted 12 days but if any symptoms of emetine intolerance were observed, a day's rest was allowed between the ninth or tenth day. The full course of 24 grains was given in all cases. The stools were examined daily for six consecutive days after treatment was completed. It was not possible to carry out any more elaborate examinations to test the permanency of the cure.

The treatment was both tedious and rather drastic for the patient, but it gave the best results for the carriers with symptoms. On the other hand a small percentage, about 5 to 8 per cent, failed to be cured. After some time it was realized that most of the failures were in cases with mixed bacillary and amœbic infections. Probably it was the acidity in the gut in this type of stasis that rendered the emetine in the cæcum inefficacious.

During my researches on quinine in 1921 I found that the lethal concentration of this alkaloid was lowered from 1-100,000 at a pH of 8 to 1-10,000 at a pH of 6. Emetine I found to be almost identical with quinine at these pH's when tested on *Paramœcium caudatum*.

The next line of treatment, which was adopted only in cases of mixed infections, was to commence immunization as early as possible with vaccines prepared from the causative organisms of the bacillary infection. After the fourth dose of vaccine, i.e., on the twelfth day, the bismuth emetine iodide treatment was commenced and the vaccine treatment continued until the sixth dose. During the vaccine treatment, up to the fourth dose, calcium lactate (10 grains) and parathyroid (1/10th of a grain), morning and evening, were administered on an empty stomach and starches eliminated from the diet.

The results obtained with this treatment were very much better and failures ceased to occur. The method, however, proved too elaborate for India, owing to the bacteriological difficulties of diagnosing cases of mixed infection. It may be necessary to plate for 4 to 5 days before the causative organism is found.

Major H. C. Brown had already called attention to the value of the kurchi bark, *Holarrhena antidysenterica* (Apocynaceæ), for the treatment of amœbic dysentery. Colonel Chopra and I considered that if it were possible to make a bismuthous iodide salt of the alkaloids of kurchi bark it might be used as a substitute for bismuth emetine iodide. Dr. Sudhamoy Ghosh prepared such iodides for us. We found they were less toxic than emetine so that it was possible to give a 10-grain dose twice a day for 10 days without toxic effects. It appeared that in this way we would be able to increase the kurchi alkaloids in the cæcum to lethal concentrations. At first the results were very good and it looked as if the bismuthous kurchi iodide was to be the solution of this problem. Unfortunately at this stage the demand for kurchi bark became so great that it became valueless from adulterations, improper picking, etc. Colonel Chopra has been working on this subject and a supply of proper mature bark will have to be obtained before the alkaloid and its bismuthous salts become a reliable method of treatment.

In the meanwhile, Dr. A. C. Reed, of the School of Tropical Medicine, San Francisco, asked us to try carbasone—an arsenical compound which Ehrlich had produced during his studies with Hata on the preparation of salvarsan 606. As I was leaving Calcutta Colonel Chopra told me that he had tried it on fifty *E. histolytica* carriers with results which compared very favourably with those obtained with bismuth kurchi iodide.

Both methods are free from toxic symptoms, are efficient, and do not require retention in hospital. Further tests will indicate which is the better of the two treatments.

Reviews

THE CLINICAL STUDY AND TREATMENT OF SICK CHILDREN.—By John Thomson. Fifth Edition by Leonard Findlay. Edinburgh: Oliver and Boyd, 1933. Pp. xxxvi plus 1075, with 344 illustrations. Price, 30s.

THE first edition of this invaluable book appeared in 1893 and the fourth and last in 1925 not long before the death of its author. As Dr. Leonard Findlay says, Dr. John Thomson was a master clinician and his book reflected the experience of a life-time devoted to the study of disease as influenced by and reflected in infancy and childhood. It is therefore an excellent thing to have a new edition of his book, enlarged and brought up to date by the hand of another great specialist in pædiatrics. The character of the original book is retained. It is written largely from the clinical point of view. The best methods of examination of the different systems in young children are described, and the significance and diagnostic worth of the various symptoms and signs are given. The volume does not pretend to be a complete treatise of all diseases met with in the child, nevertheless very full descriptions are given of all the diseases commonly met with, and many of the rarer diseases are also described and many photographs of rare and unusual conditions are included. The book runs to more than 1,000 pages. The sections chiefly revised in this edition are those on nutritional diseases in infancy, rickets, acid intoxications, tuberculosis, and rheumatic infections in childhood. The section on rickets is very full and particularly interesting. It gives a résumé of all the various theories which have been held of the causation of this widespread disease, showing how each advance in medicine has produced a new and fashionable theory. It is interesting to find that Huntly, a medical missionary in India, stated in 1889 that rickets was due to absence of sunlight, and Palm who had studied conditions in India and China also concluded in 1890 that

rickets was most prevalent where sunshine was least. Their work received little notice, and it was not till 1919 that serious attention was paid to this factor. Dr. Findlay says that we are still not certain of the real cause of rickets. Fortunately however nowadays we do know how to prevent it and how to cure it in its early stages at least. The chapter on tuberculosis is also particularly interesting. Although tuberculosis is diminishing in England and Scotland, it still remains one of the commonest and most serious of the diseases of childhood. We do not perhaps all realize that 'pulmonary tuberculosis is pre-eminently a disease of infancy and early childhood. There are more deaths from pulmonary tuberculosis during the first two or three years of life than during any other age period'. An investigation of the incidence of pulmonary tuberculosis in the infants of Bengal would be of great interest. Dr. Findlay describes how sputum can easily be procured even from young children for such an investigation.

The first part of the book deals with the general clinical examination of children, their normal development and growth including a very interesting chapter devoted to the teeth, and with the feeding of infants and older children. Several chapters are devoted to feeding. Dr. Findlay holds that where breast milk is not available the best method of rearing an infant is on undiluted cow's milk, practically from birth. The iron of milk is only just sufficient for the infant's needs, and where dilution of milk is practised there is grave danger of producing anæmia. Nutritional anæmia is also very liable to occur in any child, whether breast or artificially fed, who is kept too long (more than 10 months) on a diet consisting entirely of milk.

No better book than this could be recommended for the use of those who have the medical care of children in their hands, whether specialists or general practitioners. Its clarity, balance and wisdom make it

remarkable. It is extremely well written. The print, illustrations, and general get-up are excellent.

J. M.

THE TREATMENT OF RHEUMATOID ARTHRITIS AND SCIATICA.—By A. H. Douthwaite, M.D., F.R.C.P. (Lond.). Second Edition. London: H. K. Lewis and Co., Ltd., 1933. Pp. xii plus 132, with 4 illustrations. Price, 6s.

Nor many years ago the septic-focus theory of the cause of rheumatoid arthritis held the field, to the exclusion of almost all other theories, and the term 'rheumatoid diathesis' was ridiculed as an expression only used by grandmothers and old family physicians. But the tide was now turned against septic foci, and the author of this book—as have many other distinguished physicians—has taken this opportunity to reopen the case and to examine the question of the ætiology of rheumatoid arthritis from a broader and more reasonable point of view.

The author fails to resist the temptation of delivering a *coup de grâce* to the septic-focus theory; this he does in a manner which will appeal to the average medical reader, but the figures he quotes would not, we fear, satisfy a statistician. The other chapters are of a more constructive nature.

Though we admit that it is not essential that every medical writer should be a literary stylist, we cannot help deploring the growing tendency in medical literature towards carelessness in construction and even in grammar. This book is not a particularly bad example, but nevertheless the sensitive reader will find himself shocked repeatedly. Throughout the book, *cases* recover, consult the author, and even suffer *prodromata*. 'Actually the number of recoveries was three times as great as that which improved after removal of local infection', and 'the terms "chronic arthritis" and "rheumatoid arthritis" appear to be regarded as synonymous by some authors, thus adding further to the existing confusion', are examples that occur in the first few pages; after this the reviewer acquired a certain degree of 'immunity' against further shocks.

However, physicians will find in the book a clear exposition of the most modern, and in our opinion the most reasonable, views regarding the ætiology of both rheumatoid arthritis and sciatica, and a valuable guide to the treatment of these and allied conditions.

CUTANEOUS NEOPLASMS.—By Norman Paul, M.B., Ch.M. London: H. K. Lewis and Co., Ltd., 1933. Pp. xii plus 154, with 62 illustrations. Price, 10s. 6d.

CONTINUOUS bright sunlight day after day is now being found not an unmixed blessing and in Australia, where such conditions exist, evidence is rapidly accumulating that excessive insolation of the skin is a predisposing factor to the development of malignant disease.

The opportunity presented by the unusually large number of persons who develop malignant disease in Australia has been made use of by the author of this book, and he has produced a valuable volume on neoplasms of the skin. Although consideration of malignant conditions occupy the greater part of this volume benign neoplasms also receive their due amount of attention. The book is copiously illustrated by excellent photographs and on the whole is clearly written, but we are sorry to see that the author talks of 'tubercular' skin lesions, when referring to disease caused by the *Bacillus tuberculosis*, such a careless use of this word is especially reprehensible in a dermatologist.

To say that the book is printed and published by Messrs. H. K. Lewis and Company in their usual style will be sufficient commendation to those readers who are familiar with this well-known firm of medical publishers. The book may be summed up as an eminently useful and pleasing production.

P. A. M.

BLOOD DISEASES IN CLINICAL PRACTICE.—By Prof. Dr. P. Morawitz. Translated from the 2nd German Edition by A. Piney, M.D., M.R.C.P. London: J. & A. Churchill, 1933. Pp. viii plus 102. Price, 7s. 6d.

THIS small book is a translation from the German by Dr. A. Piney, himself a contributor of several valuable shorter books on hæmatology. This book only deals with the purely clinical aspect of blood diseases and is little more than a record of the wide personal experience of the author. It is a useful résumé of the subject giving the salient points of the diseases of the blood and blood-forming organs and as such might be read with profit by a busy practitioner as a refresher, but it cannot usurp the place of the larger books. In the reviewer's experience it is unique among modern books on the blood in that it has not a single drawing or coloured plate.

ORAL SPIROCHÆTES AND RELATED ORGANISMS IN FUSO-SPIROCHÆTAL DISEASE.—By David T. Smith, M.D. London: Baillière, Tindall and Cox, 1932. Pp. xii plus 243, with 53 figures. Price, 26s.

THIS is a very useful book dealing with one of the most important groups of anaerobic organisms, the fusiform bacilli, the spirochætes and the spirilla of the mouth and the intestines, organisms which generally do not receive adequate treatment in medical bacteriology. These organisms produce a wide variety of acute and chronic lesions in various parts of the human body. In the first five chapters the biological and cultural characteristics of these organisms are described and the rest of the book is devoted to the description, diagnosis and treatment of the various fusio-spirochætal infections. A very useful bibliography containing 822 references bearing on the subject is appended. This is a book that will be valuable to all bacteriologists as well as to the clinician.

C. L. P.

THE ADRENAL CORTEX—A SURGICAL AND PATHOLOGICAL STUDY.—By L. R. Broster, and H. W. C. Vines. London: H. K. Lewis and Co., Ltd., 1933. Pp. 94, with 4 coloured illustrations. Price, 6s.

THE publication of this little book has at last removed a long-felt want amongst English-reading medical men. The subject of the adrenogenital syndrome attracted the attention of scientific men only comparatively lately and their observations have so far been published as individual contributions, in different medical journals, both in England and abroad. We congratulate Mr. Broster and Dr. Vines for taking the initiative and placing all the facts together in this volume, for the information of the general medical profession. After a very careful and painstaking research, they have discovered a new method of study, by special histological means, of the cytology of the adrenal cortex. There was no reliable method for demonstrating the pathological condition of the suprarenal gland under the microscope and the Ponceau-fuchsin technique for the histological exhibition of cell granules of a definite character will be hailed by everybody interested in the subject. For this reason, the writers deserve our warmest thanks.

The book is divided into three parts. In the first part, the usual clinical picture of the adrenogenital syndrome with virilism and its different varieties have been described. The results of the complete investigation, including unilateral adrenalectomy, of ten typical cases have also been described. In all of them, the cortical cells gave a very strong fuchsinophil reaction when stained by the authors' technique, indicating an abnormal functional activity of the cells, which appears to be responsible for this tendency to sex reversion. In the second part, a further series of ten cases of various degrees of virilism, but without any gross enlargement of the adrenal glands, are described.

These cases show lack of development of the genital organs with cystic degeneration of the ovaries. This series includes interesting descriptions of two hermaphrodites who were brought up as females but were really undeveloped males. In the third part, the authors describe the actual technique of their special stain and also discuss the subject, on an histological basis, from several points of view. They have also given a philosophical discourse on the probable causes of sexual reversions and masculinization of females. The four coloured plates, illustrating the reaction to their special Ponceau-fuchsin staining, are excellent.

While going through the book, certain mistakes have been found. The following may be cited: Page 26, under sugar tolerance curve, .96 should be .096; page 32, under blood count, C.I.9 should be .9; under blood cholesterol, .15 mgm. should be either .15 per cent or 150 mgm.; under sugar tolerance, 15.5 should be .155 and 15 should be .15; page 50, under blood sugar curve, .9 should be .09; page 52, under haemoglobin, .96 should be 96 per cent.

Sugar tolerance (Avery) does not express anything. Apart from these inaccuracies, the book contains excellent material for study and we fully recommend it to students, practitioners and research workers alike.

M. N. D.

OTHER BOOKS RECEIVED.

The Study of Anatomy. By S. E. Whitnall, M.A., M.D., B.Ch. (Oxon.), M.R.C.S., L.R.C.P., F.R.S. (Canada). Second Edition. Rewritten and Enlarged. London: Edward Arnold and Co., 1933. Price, 4s.

Zoology. The Invertebrata. Part I. (Catechism Series.) By R. A. Staig, M.A., Ph.D., F.R.S.E. Third Edition. Edinburgh: E. & S. Livingstone. Price, 1s. 6d. Postage, 2d.

Mental Diseases. Second Edition. (Catechism Series.) Edinburgh: E. & S. Livingstone. Price, 1s. 6d. Postage, 2d.

Annual Reports

ABSTRACT OF A REPORT ON INVESTIGATIONS INTO THE PROBLEM OF OEDEMA IN SIERRA LEONE. BY W. A. BURNETT, B.Sc., M.B., Ch.B., D.T.M. & H.

A PATHOLOGICAL condition diagnosed as the oedematous type of beriberi has been present for many years in Sierra Leone; at intervals outbreaks of epidemic severity with a high rate of mortality occur.

The problem of beriberi is one which has been noted in Freetown Prison for at least the last forty-eight years. At this institution it had been reported under several diagnoses, to wit, oedema, dropsy, beriberi, dysentery with dropsy. Various spasmodic references have been put on record until recently when an investigation was made by Professor Blacklock in 1922, and later in 1929, when Drs. Leitch and Watson undertook an intensive and exhaustive survey of the condition at the Freetown Prison. The outcome of their work was that drastic alterations in management were suggested, together with the allowance of a diet very rich in vitamin B and of high calorie value, as much as thirty-five hundred calories being allowed to adult male prisoners on sedentary occupation. 'There is no excuse for its existence, as it can be guarded against by easily arranged and inexpensive measures; given an adequate diet, all that remains is to see that the vitamin B content of the diet remains up to standard', quote the joint authors of 'Beriberi in the Freetown Prison'; yet despite the most strict adherence by the superintendent of prisons to this dietary advice, coupled with the daily inspection of the inmates' food rations by the prison doctor, the medical officer in charge of Freetown Prison continued to find this 'oedema' cropping up among the prisoners and culminating in a severe outbreak in 1931. A diet rich in yeast, cod-liver oil, fresh vegetables and fruits, despite the reputedly high content of vitamin B, had failed to prevent a serious recurrence of the condition. At that time large quantities of marmite and bemax were being given without the success one would have expected from these 'vitamin' foods, if the condition had been one purely of avitaminosis. It was only after an alteration of the diet to consist of new rice, a step suggested by Mr. Biddle, the superintendent of prisons, from his lifelong experience of the condition, that a mass improvement set in and no new cases were reported. It seems a great pity that his valuable first-hand knowledge of this disease does not appear to have been utilized to better advantage in some of the previous epidemics.

During the period from August 1931 to January 1932, there was a very considerable outbreak of the oedematous condition here, involving Freetown Prison, Wilberforce Barracks and Kissy Asylum. A number of Freetown inhabitants, too, complained of the disease and were treated at the Connaught Hospital.

The condition clinically.—The syndrome takes the form of a varying degree of non-albuminuric oedema, usually well defined in the limbs; of dyspnoea on the minimum exertion and of tachycardia with enlargement mainly of the right heart; of muscular weakness with deep muscular hyperaesthesia; of gastro-intestinal disturbances, generally constipation, sometimes followed, in the fatal cases, by diarrhoea and faecal blood, and of such nerve changes as are displayed by diminution of, or loss of, tendon reflexes, localized and often transient anaesthesia and deep hyperaesthesia. Difficulty of vision is present at times. There may be, and generally is, a slight pyrexia, but the fever does not usually exceed a range of 99°F. to 101.5°F.

The blood examination does not reveal any obvious pathological change. There is a slight hydremia associated with diminished red cell count (average 4,300,000 per c.mm.) and with a lowering of the haemoglobin content to 70 per cent. The colour index is generally found to be in the region of 0.81. Although the white cell count ranges from a value of 7,000 to 11,000 per c.mm., the most marked change in this aspect is the decided shift to the left in the Arnetz index. Quite a considerable proportion of bilobed and trilobed polymorphonuclear leucocytes is to be seen.

Records of the blood pressure are found to vary in the people affected in accordance with the state of the bowel and of the heart. During the phase of subacute or chronic constipation, there is a definite elevation to 150-170 mm. Hg. systolic (90-106 mm. Hg. diastolic) but when recovery sets in or the intestinal stasis is relieved for a few days this blood pressure steadily falls by 20-30 mm. and is maintained at a lower level, 130-140 mm. systolic (70-84 mm. diastolic). Where the signs of pericarditis with effusion are present coupled with diarrhoea, the blood pressure is constantly low (100 mm. systolic, 60 mm. diastolic); when these patients are recovering, which they do very slowly, the blood pressure is equally tardy in rising to the normal and, in the cases under review, no one exceeded a final reading of 118 mm. systolic, 72 mm. diastolic.

The urine shows none of the ordinary abnormalities. It is free from sugar, diacetic acid, acetone bodies and albumin, but although just slightly diminished in

amount it contains an excessive quantity of phosphates, which separate on cooling.

WILBERFORCE BARRACKS

The conditions at Wilberforce Barracks, where are stationed soldiers of the Royal West African Frontier Force, render the study of epidemic and general diseases much simpler than among the general African populace.

The barracks.—The barracks' compound is situated on a hill sloping fairly gently downwards in all directions. The lines of huts are placed in parallel rows running north and south. The huts occupied by the soldiers are of mud construction, measuring over all 45 feet by 34 feet. They are separated from one another by a minimum clear space all round varying from 18 feet to 33 feet wide. On each long side is a verandah 6 feet wide. The huts are subdivided by mud walls 8 feet 6 inches high and 6 inches thick, into eight rooms each measuring 10 feet square. The walls do not extend to the roof, which, at the highest point, is 11 feet. A ceiling is formed by stretching over the top of the walls a horizontal layer of wide-mesh wire netting. The floors, including the verandahs, are built up 3 feet 6 inches above the ground level. Each room has one window, capable of being opened, and one door, but in some of the huts the partition wall has been cut to make an internal communication between adjacent rooms. During the day the rooms are cool, chiefly on account of the covering of thick thatch on the corrugated iron roof, which is carried well down over the verandah to provide shade and to reduce the ingress of reflected heat from the ground. All the rooms are more or less infested with bedbugs (*Cimex lectularius*, *Leptocimex boueti* and *Cimex rotundatus*) and the possibility of migration, not only from room to room, but from hut to hut, is far from remote.

Cooking.—Generally, the cooking is conducted in communal kitchens, which are huts with freely opened partition walls. Individual fires are employed and the cooking is conducted by the women, who use the kitchens as convenient places wherein to beat the rice by the native mortar and pestle method.

Latrines.—The latrines are well isolated and at least fifty yards from the huts of the compound. Men and women use separate buildings, which are erected to accommodate the dry bucket system. The faecal matter is buried in a large pit, 200 yards from the nearest hut and to the prevailing leeward side of the compound. These conveniences are kept clean and tidy and are inspected regularly by the sanitary inspector allocated to the barracks.

Drainage.—Open surface gutters are in use for drainage with water channels running away from each hut. As the compound is built on rock on an exposed sloping hill the drainage is ample, well designed and sufficient.

Water supply.—The water supply is brought in by pipe line from the hill station supply and laid to convenient automatic stop cocks; no waste is permitted.

Rubbish bins.—Small rubbish bins with steel lids are located near the water taps (about 20 feet from each one). These appear to be used with disciplinary care, as no evidence is visible of indiscriminate scattering of rubbish and there are sufficient bins to accommodate the refuse without piling it up around the receptacles. They are emptied daily and the rubbish is incinerated.

Wash-houses.—Wash-houses are separated from the compound on the eastern side of the hill.

On the whole the compound is tidy, well kept and efficiently managed, as far as sanitation is concerned.

The epidemic

At the end of October 1931 the disease was first brought to notice by a soldier complaining of swollen legs, constipation and breathlessness on exertion. His heart sounds were soft and muffled but there were no valvular murmurs. The urine displayed no abnormalities

(albumin, sugar, acetone bodies) but it contained an excessive amount of 'earthy' phosphatic deposit. It was considered advisable to have the man admitted to and treated at the Connaught Hospital where, however, he died two days after admission. He had been ill for seven days.

The necropsy revealed acute pericarditis with effusion (8 oz.), cardiac enlargement, pulmonary oedema, scanty volume of fluid in the peritoneum, hepatic oedema, enlarged gallbladder with normal bile, and oedema of both legs extending only to the knees. The cause of death was diagnosed as beriberi of the wet type and pericarditis with effusion.

Survey of troops.—On account of the presence of beriberi at Freetown Prison and of the information that the troops were being issued with rice from the same contractor who supplied the prison, it was deemed essential to take urgent measures to round up all affected soldiers. Consequently, a survey of the entire personnel at the soldiers' compound was undertaken to isolate similar patients and to anticipate early cases.

All the huts and rooms were numbered and a plan was made of the compound, showing such details as position of huts, kitchens, latrines, drains, rubbish heaps and water supplies. Small metallic discs were figured with the hut and room numbers. They were issued to the responsible occupants of each room, with the instructions that on any complaint of sickness by any inmate, such patient should appear with the disc at the morning sick parade, so that any disease, whether of an infectious nature or otherwise, could, by comparison with the numbered plan at the medical officer's hut, be localized immediately and, if need be, suitable steps taken at once. The misuse of discs by persons is an offence punishable on the owner of the disc, and loss of disc is notifiable immediately.

A census of the soldiers' lines in the compound was made.

The oedema cases.—The serious cases of oedema were admitted, some to the Connaught Hospital but others chiefly to the hospital at the barracks, where they were treated along several lines to find, if possible, an efficient remedy. In the barracks' cases the diet was kept unaltered and consisted of rice seasoned with red pepper, palm oil and, occasionally, with the addition of a small piece of beef or fish.

The other patients and early cases were grouped as ambulatory subjects in experimental classes and various prescriptions were given each group, with the possible object of obtaining better statistical data concerning treatment.

All these subjects were given medical treatment daily for an observation period of eighteen days and the results were noted. They remained on the same diet to which they had been accustomed and no new rice was allowed, nor was there any special issue of foods rich in vitamin B. If improvement did not follow within eighteen days the subjects were switched over to a line of treatment which had been proved to be successful for other groups. Thus, in some classes, no betterment was observed, in fact, many patients became worse but when given the 'calcium lactate purge' mixture or calcium lactate and sodium citrate, they all cleared up rapidly in ten to twelve days. No fatal issue attended the experiments although many ambulatory subjects had well-defined oedema.

Hospital cases.—Generally, the patients treated in the hospital cleared up more rapidly due to the rest in bed and to the better conditions of warmth and shelter maintaining in the building.

The food of these patients was what they had been having in their huts at the barracks' compound, where it was prepared and then brought over to them. They each consumed daily about 1½ lb. rice, cooked with the addition of red pepper as curry, palm oil (about 2 ounces) and some dry fish.

Very few of these patients received beef every day but they all had it twice a week. On other days the

protein was obtained in the form of dried fish. In general, as far as protein-rich food-stuffs is concerned, the average soldier lived on what may be colloquially termed the 'hunger and burst' principle. The meat ration is reduced to a minimum till the week-end and, especially, till pay day at the end of the month, when, at Wilberforce Barracks, extra cattle are killed to supply the market demand. It was fortunate that the majority of the hospital cases did not receive the surfeit of beef during their stay in the hospital. As will be shown later, excessive amounts of meat have a peculiar influence on the course of the disease, in that the oedema tends to be reduced with a diet rich in animal protein. This aspect of the condition was confirmed by observations on the inmates of Freetown Prison.

Treatment survey.—Surveying the treatments, it was considered that, to be successful, it was necessary to include calcium lactate, preferably made easily assimilable by exhibiting also the alkaline effect of sodium citrate and to add an efficient saline purge. Although, however, this calcium lactate and purge treatment made the oedema vanish and enabled the patient to feel well and to be able to resume duty, it cannot be considered a cure provided the subject continues to eat faulty rice. So long as this type of treatment is taken, the rice could be consumed without any considerable increase of the oedema following, entirely, I think, because of the purging effect of the saline and of the vasotonic influence of the calcium salts. When the treatment was withheld the dropsy returned in about eleven days and it was always preceded by a bout of constipation. On the other hand the treatment effected a permanent cure of the condition after six months, when the men ate new season's rice, even despite the onset of attacks of constipation or when the 'oedema-producing' rice was cooked as I directed.

Distribution of cases.—Concerning the distribution of oedema among the entire colony at the compound, the table below demonstrates the age and sex incidence:

Total cases	.. 54	Men	.. 30 : 226	13.3%
" population	554	Women	.. 19 : 185	10.3%
" incidence	9.7%	Servants	.. 4 : 63	6.3%
		Children, boys	1 : 31	3.2%
		Children, girls	0 : 49	0.0%

Among the entire inhabitants, the incidence of oedema was 9.7 per cent with a sex and age distribution as shown above.

That the soldiers are exposed to the strain of physical training, to drill in comparatively heavy equipment and to strict discipline are potential causes of the high relative incidence of the condition among their numbers. Women do not lag far behind in that they have fairly hard work to do washing clothes and preparing rice by pounding in the native mortar with heavy wooden pestles. The boys (servants) come under a special category. Some are attached to the native soldiers and others to the European officers. Among the latter no oedema was observed; whether or not this is due to the lavish treatment by their employers or to the enhanced opportunity of participating at a better commissariat is unknown, suffice it to remark that none of these boys showed any signs of chronic starvation and they did not eat the same rice as was consumed by the soldiers.

The female children, by a close association with their mothers, are better looked after than the male children. This may be the cause of their increased resistance to the condition.

Multiple infection.—Infection ought to be considered in terms of multiple infection, where two or more people in the same room exhibit the sickness at the same time. Forty cases were found in rooms occupied by more than one individual, yet, although the total number of occupants of these rooms amounted to ninety-eight, only seven cases of 'dual' infection occurred.

Of the forty, thirty-three were married people but of these only five couples were found to be suffering at the same time. In one case a man and his child were affected and in another two of three sisters, so that, in

all, seven instances of 'dual' infection were displayed, that is, the disease affected only fourteen people, who were daily in the closest contact with their neighbours. During any part of the work there was no indication of one individual being affected and a neighbour later after a definite incubation period. This idea of infection by contact and by vectors had carefully to be considered because of the peculiar suspicion of an infective agent in the prison cases. It will be brought up again later.

The theory of an insect vector merits further attention, when the loci of the disease are considered along with the plan of the compound. The bulk of the cases was confined to huts, which are all situated together. The possibility of an insect vector disease became apparent, but, as the work progressed, it was partly relinquished in view of the theory of rice poisoning expounded later. After all, even allowing the chance of a disease being carried, these people were all, more or less, eating the same food which, if proved to be toxic, would eliminate the necessity of considering an insect-borne disease. It is considered superfluous to promulgate theories of infection and of insect vectors, if in a mass attack all the members of a community partake of the same type of food, which is shown to be detrimental to health.

Rice at Wilberforce Barracks.—At the time of the outbreak, I examined, in conjunction with the superintendent of prisons, specimens of rice supplied to the Royal West African Frontier Force. The samples had a musty smell. I found the rice to contain a high percentage of old dead and fungoid-diseased grain (29 per cent) and to be mixed with a small percentage of bored and broken grains. Weevils, rice bugs and maggots were present. A large percentage of the rice showed black and dark brown discoloration, extending from the pericarp inwards to the starch.

The soldiers complained that when they ate this rice they suffered from colic and abdominal trouble, some with constipation, others with diarrhoea. In all cases of oedema at Wilberforce Barracks, there was a history of gastro-intestinal stasis occasionally with colic.

Effect of washing rice.—To make it a safer food, I recommend that the rice be cleaned in water and cooked in a special manner. This consists of washing thoroughly in cold water, placing the rice in a pot with water to cover, just bringing to boiling point and throwing away the yellow-brown boilings. Fresh clean water is then added and cooking is continued till the rice is soft and edible. By these means it is maintained that soluble toxins are dissolved and thrown away but any vitamin B is retained undestroyed. A number of women in the compound had been using this method before I recommended it and in no case was any of their family circle affected. On the other hand, in every case of oedema, although quite a number washed the rice in cold water before cooking, all invariably conducted the cooking of the rice by adding just sufficient water and boiling till the grain had softened and absorbed all the water. There was no mention of throwing away the initial boiling water. Recovery from the oedema became permanent when this method was adopted.

One case is of special interest in this consideration. A patient (a) had been admitted to the barracks' hospital and treated with calcium lactate and sodium citrate. In the hospital he shared the rice of another patient (b), a case of bronchitis, whose wife threw away the first boilings. Both men recovered and returned to duty but a fortnight later (a) was readmitted to the hospital where he informed the dresser that he had gone back to his own wife's method of cooking, in which all the water was boiled into the rice. (a) recovered and did not show any relapse to the oedematous condition, when he consumed the rice after the initial boiling water had been rejected.

Previous outbreaks.—On account of the difficulty of obtaining accurate data, any reference to previous outbreaks of oedema at Wilberforce Barracks is scanty.

The daily record of medical complaints was gone over for the last three years in the hope of glean some such information.

Although there is a fairly constant relation between constipation and œdema (constipation always preceding œdema), the same does not necessarily apply to rheumatism. This may be merely a question of nomenclature. The terms myalgia, rheumatism, lumbago, sciatica, fibrositis, muscular and joint pains have all been employed and it is difficult to know if previous medical officers considered rheumatism in the narrow sense of 'joint pain' or if they imply the aspect mooted by Professor R. Stockman of Glasgow University of a disease essentially of overgrowth and inflammation of the fibrous tissue, no matter where disposed this essential packing tissue may be.

In general, Drs. Leitch and Watson's work confirms these observations on the correlation between rheumatism, œdema and constipation, although they do not indicate that gastro-intestinal disturbance may be a forerunner of beriberi œdema.

I am told, too, that the late Dr. Young commented on the correlation between gastro-intestinal disturbance and dropsy, when he was medical officer at Freetown Prison.

Mr. Biddle's experience, also, is most helpful. He states that he does not remember having seen a case of beriberi that was not preceded by a history of gastro-intestinal upset, taking the form of constipation and later of diarrhoea.

The last epidemic had been present at the Freetown Prison and at Kissy about August 1931, but it did not break out to any extent among the Royal West African Frontier Force until early October 1931, when it rose rapidly to a peak value in November and steadily declined. It has since disappeared (January 1932). From information received from Mr. Biddle, there definitely was an issue of diseased rice to the Royal West African Frontier Force in July 1931. Any inferred incubation period cannot, however, be set because the troops drew this rice from the quartermaster's store as required, therefore, of necessity, the stocks held by the soldiers were of variable amounts. Good rice has since been issued to the troops and no new cases of œdema have occurred.

Outcome of the work.—The inhabitants of the Wilberforce Barracks' compound continue their simple diet of rice, palm oil, pepper, curry, with an occasional portion of fish or beef and a small amount of fresh fruit. No added vitamin products like beimax, marmite, yeast and cod-liver oil are taken with the food. They live an open air life on an exposed part of the country. Essentially, their conditions are the same as they were during the outbreak of œdema, yet merely since changing the rice and/or method of cooking, œdema has been reduced here to the vanishing point by employing these simple means, and by ensuring that, through the quartermaster's department, a supply of good sound rice is issued to the troops.

All the patients who contracted the disease during the last epidemic have since been examined at intervals and found to be well. There is no evidence of permanent injury in the way of œdema, cardiac disability or nerve changes. In my opinion, this cannot be claimed simply as a victory for treatment by calcium salts and by purging alone but I consider that it is of foremost importance to ensure that these people are supplied with rice in good condition and not showing signs of deterioration.

KISSY ASYLUM

During the enquiry, this institution was under the charge of Dr. Easmon, who kindly assisted me, as far as possible, with statistical data concerning the condition at the asylum. There was no history of any previous outbreaks but during the present epidemic no less than twenty deaths occurred from August to December 1931.

Although I was responsible only for the post-mortem examinations and I performed the majority of the

necropsies, I made a few observations on the housing conditions and on the diet of the inmates.

Accommodation.—The majority of the patients were accommodated in large wards, with beds the regulation distance apart and without overcrowding. The clothing and bedding were clean and did not show signs of verminous infection. The walls of the wards were made of a mud-cement composition, parts of which had been broken in places. No bedbugs were found. There did not appear to be evidence of any patient having the infection carried from his immediate neighbour, as will be presented in cases which occurred at Freetown Prison. In general, the inmates were clean and showed signs of kindly treatment and good care.

Dietary.—At the same time I visited the kitchen of the asylum and inspected the rice bin, where there was stored a quantity of rice containing old fungoid grains, bored and broken grains and discoloured grains. Weevils and maggots were seen in the bin. This rice contained on examination 33 per cent of pericarp as shown by the Vedder and Feliciano method. The rice was supplied from the Freetown Prison and came from the same source as was used in Freetown Prison and Wilberforce Barracks.

The inmates of the asylum had their rice cooked in a large open boiler, into which the grain was placed, water added and boiled for twenty-five minutes. Any surplus rice water was not discarded but was added to soup, although the cook informed me that generally the water more or less all boiled into the rice. During the epidemic there was no doubt that Dr. Easmon relying on the diagnosis of beriberi due to avitaminosis did all in his power to cope with the condition by allowing a most liberal diet, high in calorie value and excessively rich in added vitamin products. This had not the slightest effect on the course of the epidemic.

Observations.—In the course of my duties, I interviewed several inmates. In November I found eight cases of œdema most of whom came ultimately to necropsy before the year ended.

On enquiry, I learned the treatment consisted of a very liberal diet of rice, greens and meat, with marmite as an additional source of vitamin B. To the patients suffering from pericarditis a cardiac mixture called 'mist. beriberi' was exhibited.

Unfortunately, in all the cases I saw, it did not have the desired effect, even when coupled with large doses of vitamin B (supplied in the form of marmite). However, as my duties did not extend to treatment of the cases, the observations I made at Kissy Asylum, where the outbreak was very serious, were confined to post-mortem examinations.

HOSPITAL CASES

Out-patient department.—In November 1931 many cases of œdema cropped up at the out-patient department. They displayed the same signs as were present among the troops and among the prisoners at Freetown Prison. Œdema of feet and legs was commonly coupled with a history of chronic constipation. The urine showed no abnormalities but had an excessive amount of 'earthy' phosphates which, in these cases, may have been due to reduced water intake with the concomitant result of higher concentration of urinary salts. Many had præcordial distress and breathlessness. In one man, a pauper, who had been consuming black mouldy rice, œdema of the abdominal wall and of the skin over the sternum was found in addition to dropsy of the lower limbs.

All the cases were requested to furnish samples of the morning urine and of the rice which they generally had been using. Thirty-six cases in all were observed.

One young girl (aged twelve years) brought a new sound rice, which turned out to be recently purchased, as she did not like to show the old rice which she had been eating. Two patients, sisters, had been for several months eating parboiled rice, in which the grain was large and white with no pericarp remaining. They were treated as cases of true beriberi avitaminosis.

They were given cod-liver oil, fresh tomatoes and other fruits and advised bema, upon which the condition slowly abated. They became perfectly well after eight weeks treatment, but it was learned they had commenced to eat, during the course of their treatment, new season's rice, of which they brought a sample. It was not parboiled and contained 58 per cent pericarp.

A fourth subject was admitted to the hospital as a case of dry beriberi. He had been serving on board a ship on which he stated old rice had been issued. He improved on a full diet of bread, butter, meat, fish, eggs, milk, potatoes, fresh fruit without additional accessory food substances and he was discharged with complete recovery four weeks later.

In the remaining thirty-two cases treated, all the rice samples examined were of poor grade, containing discoloured grains, fungoid grains and signs of weevil activity. These subjects were all treated by the calcium lactate and purgative method and all cleared up within twenty days of treatment; at least after sixteen days they showed considerable improvement, had their mixture repeated and did not report again, except for four cases whose improvement was sluggish but positive and who disappeared after twenty-eight days under casual observation.

All these subjects in the out-patient department were advised about rice and cooking and most of them stated they used up their rice stock by altering the cooking.

In-patients.—Twelve cases were admitted for observation. Urinary examination in all cases but one revealed no albuminuria or other of the customary abnormalities but at first all had excessive phosphates. The one exception was a case of subacute nephritis with albuminuria and casts. In the remaining eleven, there was a constant history of chronic constipation, rheumatic pains, slight palpitation and breathlessness on exertion, tender calf muscles and oedema of the legs to the middle of the thighs. Ten had partial anaesthesia (loss of heat, tactile and pain but not of cold) over the pretibial area. The remaining one had diminished sensation only to touch and temperature, pain being present. The tendon reflexes were variable. On admission, they all had slightly elevated blood pressure (average systolic 152-164 mm., diastolic 90-106 mm.) and with the rest in bed and treatment this was steadily reduced (systolic 123-142 mm., diastolic 80-81 mm.). Two cases complained of difficulty with vision and of photophobia. One had increased intra-ocular tension and signs of early glaucoma, which, however, cleared up on treatment.

The diet was standard for all these patients, termed 'full hospital diet', which was composed of rice, greens, beef, tea, sugar and dry bread. The medical treatment was grouped as at the Wilberforce Barracks Hospital:

Results.—These eleven patients reported in one month after discharge and all remained normal, except one, who had been unable to purchase good rice or to have his food properly cooked.

Reverting to the Connaught Hospital groups (a), (b) and (c), it was shown that in:

(a) Calcium lactate and iron tonic there is a tendency to constipation which is considered to be responsible for the delayed recovery.

(b) Calcium lactate and purgative act almost as rapidly as simple enemata but at Connaught Hospital the recovery period is faster than at Wilberforce Barracks where the diet is of poorer quality and less liberal.

(c) The enemata results are of interest. These subjects were allowed (group C-1) the same diet as the others in groups (a) and (b) but they had twice daily a simple water enema without soap, using a quart of water each time. Copious foul-smelling results were obtained at first with hard inspissated faeces. After four treatments the washings were returning clear, except with traces of mucus. The odour had almost gone and the patients were looking obviously improved. The expression was brighter, the eyes less sallow and, most annoying of all it was with difficulty that they

were persuaded to remain in the hospital, possibly an aftermath of the strenuous treatment. In group C-2 enemata and diet, with rice replaced by bread and potato, the speed of recovery was the same.

FREETOWN PRISON

Oedema has been present in the Freetown Prison for at least the past forty-eight years and notifications have repeatedly been made to vague outbreaks of a condition of dropsy with dysentery. It has been only within the past few years that the disease has been labelled 'beriberi', especially when the final stages of the condition have been observed. Recently the work received intensive study in the hands of Professor Blacklock and Drs. Leitch and Watson.

Previous work.—Mr. Biddle's observations are those of the layman, unbiased in outlook and unsteeped in the lore of medical diagnosis. As such, I think they have to be considered with respect, especially also, as he has had constant contact with the disease for at least eighteen years. He has remarked that all the epidemics occurring at the prison since 1914 have invariably been preceded by gastro-intestinal symptoms, chiefly of a dysenteric nature.

The particular causal agent, whether bacterial or otherwise, has never been determined with any measure of success, and Drs. Leitch and Watson were unable to track down any organism to which might be attributed the disease. They refer to one case, in which they found only the common organisms (*B. coli communis*, *B. megatherium*, *B. friedlanderi* and *B. morgani*) to which none of the pathological findings were attributed. They came to the conclusion that this disease was definitely due to 'B' avitaminosis.

The superintendent of prisons makes a valuable observation, in that, if within a few days after the beriberi had been diagnosed, the patient developed a mild attack of diarrhea, he usually died, whereas all the cases who suffered from a prolonged and severe attack of dysentery recovered from the beriberi condition. These curious phenomena had also been commented upon by Dr. Butler in 1914 and the late Dr. W. A. Young in 1919. Young went the length of isolating every person on admission until he was proved free from infectious disease. In view of the purging effect of the treatment I adopted at Wilberforce Barracks and at Connaught Hospital, this observation is of great interest in that a similar absence of intestinal stasis is the net result both of treatment by purgatives and of chronic dysentery.

Theory of infection.—Commenting on the possibility of an infectious disease, the superintendent of prisons states that during the last epidemic (1929) the first patient was an assistant warder, Lamina, who was in charge of the carpenters' workshop. He died after about ten days' sickness. The next case, also fatal, was a prisoner, Sandi, who worked under Lamina's supervision. When the epidemic was almost at a peak, another warder, Yamba, took ill after he had been allocated duty at 'D' block, where the majority of the cases were under observation. In this subject a long history of dysentery of two months' duration was noted and, although he made a remarkable recovery, he was no longer fit for the service.

Continuing his observation, Mr. Biddle makes note of a prisoner, Abu Lemberg, who had been recommended for the radical operation for double hernia. On account of his poor state of nutrition, he was admitted to the hospital and allowed a liberal diet. His physical state became so much improved as to enable him to be fit for the operation but, just at that time, two epidemic cases were admitted to the hospital and confined to beds on either side of his. A few days later, in spite of his most liberal diet, including tomatoes and other fruit, Abu Lemberg developed the disease from which he managed to recover.

Mr. Biddle makes reference to the large number of cleaners who suffered during this (1929) epidemic. Although normally eighteen are allocated to the task

of removing, emptying and cleaning the commodes of the entire prison, the incidence of cases in this section was very high, as instanced by the fifty-six who suffered in a population of 218 men. It was considered that there was a grave risk attached to this work and even the men themselves had the impression that it was of a deadly nature. The superintendent of prisons tells me of one man, who belonged to a particular group under survey, and to whom this task was allocated. The prisoner did not remonstrate but merely remarked to Mr. Biddle that if instructed to do so he would perform the job but 'he go die'. A short time later the man fell ill with the epidemic sickness and succumbed. However, this may have been but an example of the native's fatalism.

On their face value these incidents would appear to support a theory of infection but sight must not be lost of the point that all the men were participating in the rice common to everyone's diet and that the cleaners, who suffered most, also had the hardest physical work to perform, which might possibly be sufficient to overstep the low threshold that the average African native shows towards disease. Hard physical exercise had been recommended in the treatment, an outcome of the theory (Leitch) that oedema attacked chiefly the sedentary workers. Many untoward and fatal consequences have resulted following this advice.

Coupled with the case of Abu Lemberg are the following two incidents to display that, despite the diet rich in vitamins and of high calorie value, the spread of the disease was not retarded by taking care of calories and vitamins alone. Prisoner V. Caulker had had, over a long period, an extra ration of one pound of bread and one pint of milk in addition to his ordinary full diet, yet he was badly affected. Prisoner Sherka was granted extra bread (one pound daily) on account of his old age but he, too, developed the disease.

When I took over the Research in November 1931, my work did not permit of treatment or of intensive experimental observations on the patients, who were under the control of the medical officer in charge of the prison and the time had to be devoted to such aspects as were included in the biochemical and biological research. In the early stages, any work consisted of collecting samples of rice, pericarp and dust and of observing the food of the prisoners.

The rice mill.—Freetown Prison possesses the only power mill in the colony and all the rice used by the prisoners is treated here. From the contractors it is supplied as 'paddy' or rice in the husk which, before being fit for use, is cleaned by the mill, decorticated and polished partly to remove the pericarp. The end-products of milling are husk, powdered pericarp and cleaned rice, polished to any desired degree. There is a very large amount of dust in the atmosphere at this mill. This dust was collected from the walls and from the machine parts for analysis. On the whole, no sand was present among the fine floating particles. It is found chiefly in the deposit of pericarp dust in the mill and some with the husk deposit.

As many complaints of bronchitis, sore throat and gastritis are made by the prisoners who work the mill, they are supplied at the end of each shift with stimulating cough mixture. The expectorated sputum contained small particles of rice cortex with pericarp dust embedded in the desquamated pulmonary epithelial cells. Had silicosis been present, sand particles would have been present in these macrophage cells, but none were found. Phthisical sputa were not found.

The diet of the prisoners.—The diet recommended by Drs. Leitch and Watson which was drawn up expressly for its anti-beriberi value and its high calorie value is tabulated below:

Food-stuff	WEIGHT OF RATION	
	Ounces	
5-30 A.M.—Cocoa	$\frac{1}{2}$
Sugar	$\frac{1}{2}$
Wholemeal bread	2

10-0 A.M.—Foofoo (cooked)	..	24	
Beef (liver)	2	
or fish	2	
Greens (leaf)	2	
or fresh yeast	1	
and tomatoes	1	
Fresh yeast	2	
or tomatoes	2	
Onions	$\frac{1}{2}$	
Palm oil	1	
Cod-liver oil	1	
Pepper	3/80	
Salt	$\frac{1}{2}$	
Kaindah	a trace	
Fresh banana, orange, mango	1	
or pawpaw	12	
4-0 P.M.—Rice (raw)	2	
Beef or fish	4	
Yam or cocoa yam or sweet potato	2	
Ground nuts	2	
or dried beans	2	
or dried peas	1	
Tomatoes (fresh or tinned)	3/80	
Pepper	$\frac{1}{2}$	
Salt	a trace	
Kaindah	a trace cooked	
Rice, millings	in soup	
Fresh lime	a half	
Protein ..	3.26 oz.	Carbohydrate ..	17.2 oz.
Fat ..	3.4 oz.	Calories ..	3,347
			(increased later to over 3,500)

I have observed that strict adherence is being made to the new dietary. The quantities are measured with care and accuracy and, when recommended, liberal extra rations are allowed. Judged on accepted standards of vitamin value, there is no doubt but that the diet of the prisoners at Freetown Prison is probably the richest 'vitamin' diet in the colony, coupled with an intake of over 3,500 calories, suitable even for men doing heavy work in temperate zones. I am convinced that comparatively few of the general populace in Freetown, except the relatively well-to-do classes and the in-patients at Connaught Hospital, are as well fed. The prisoners have commented to me that they have never had such good and copious food in their lives.

The meals are supplied regularly, warmed and served from clean dishes in clean and tidy surroundings. Unfortunately, despite the fresh meat, greens, spinach, yeast, tomatoes, cod-liver oil, fresh fruit, sweet potatoes and ground nuts, beriberi continued to crop up in the prison.

Recently, since my appointment as medical officer in charge of Freetown Prison, I have had the opportunity of repeating some of the work done at Wilberforce Barracks and of securing new data along experimental lines.

One week before I took over the prison, the superintendent informed me that owing to shortage of supplies, he was obliged to revert to the remaining stock of old rice, containing a high percentage of discoloured grains. I concurred with his apprehension that he would surely have an outbreak of oedema. Within twelve days the complaints of pain in the chest with gastric troubles began and there were twenty-two cases of the disease noticed in the following fortnight, six of whom had to be admitted urgently to the hospital, where they made a rapid recovery. Six weeks after the issuing of the faulty rice, new grain was obtained and the disease completely disappeared in five days. The oedema subsided and no fresh notifications were made.

Outbreak of oedema.—The work was directed specially to enquire into the influence of old, 'sweated' and fungoid rice and a fortunate opportunity arose for the work. The superintendent of prisons had in the store a large stock of old rice, part of which had been issued to Wilberforce Barracks and to Kissy, and which, at

Freetown Prison, had been held responsible for the present epidemic. Although condemned it was still kept in storage. Up to December 1931, when the epidemic had been lasting from the time the supply of a mixture of new and old musty rice was delivered in 1931, there had been many reports of the sickness. About January 1932 new season's rice was obtained and this was milled, part-polished and issued to the prisoners. The epidemic subsided and the cases of oedema steadily cleared up.

The stock of new rice became exhausted, however, and the contractor delivered a large quantity of new season's rice, mixed with the old grain, which from its appearance had probably been in moist storage for a long period. Some of the rice was over one year old and it certainly was not new season's rice. This was milled and polished in the usual way. The rice contained a fair number of weevil-attacked grains and a large number of black fungoid grains and broken grains. I examined this rice and condemned it, but, for lack of other substances, part of it was fed to the prisoners. Seven days later there were complaints of constipation and pain in the precordial and epigastric regions and twelve days after the issue of this faulty rice there appeared four new cases of oedema. Three days later there were three other cases, all of whom were admitted to the prison hospital for observation. At the time Mr. Biddle assured me that if I wanted oedema cases I would be absolutely sure to get them after the issue of this diseased rice. His prophecy was borne out. On inspecting the men I found eight ambulatory cases distributed indiscriminately among the men (one tailor, one light labour, one mill, two stone breakers, three carriers). All complained of constipation. There was no evidence of nephritis but the general symptoms set out above were observed. They were diagnosed as cases of epidemic dropsy. During this small outbreak, I recommended that the boilings from rice (rice water) should be discarded and not added to soup or given to the prisoners in any form, coupled with the suggestion that the rice be more highly polished to remove the diseased pericarp. The epidemic has subsided and no new cases have been reported.

The observation that the rice be kept fairly highly polished, leaving about 15 per cent pericarp, was based on the laboratory findings of which details are given below. Mr. Biddle had noticed in a previous epidemic that there were fewer cases when the rice was fairly highly polished but no explanation of this point had been suggested.

The cases of oedema sent to the hospital for observation and treatment were taken along lines similar to those at Wilberforce Barracks Hospital. All the patients admitted displayed the characteristic signs and symptoms, including precordial pain and nausea, tachycardia, breathlessness on exertion, oedema of the legs with altered cutaneous sensation, deep muscular hyperaesthesia and constipation. The knee-jerks were present in all except one. One complained of his failing eyesight, with pain in the eyes, in which the intraorbital pressure was slightly raised. He cleared up after twenty-four days' treatment. The blood counts were variable, three being normal and three showing a slight hydramia.

The blood calcium was definitely lower than normal (10 mg. per 100 c.cm.) and amounted, on the average of four, to 7.6 mg. per 100 c.cm. In all of the cases, the pulse was increased in tension, without evidence of vascular disease, the blood pressure ranging from 156-168 mm. systolic and 94-102 mm. diastolic. With rest in bed these values fell to 130-134 mm. systolic and 80-84 mm. diastolic. One week after resumption of their tasks the pressures were still low and normal.

Two of the cases had liq. adrenalin hydrochloride (3 c.cm. of 1:1,000) injected experimentally into the oedematous zones of the legs. Localized diminution of the dropsy followed but no generalized improvement of the condition was the result.

In the treatment of these prisoners, two were given calcium lactate and purge and showed improvement

with return to labour in nineteen days. One was a case of myoendocarditis, with mitral stenosis and biliary cirrhosis. He was prescribed digitalin and, although an old case of 'heriberi' reported by Dr. Leitch, he was not considered as such for the purposes of this work. Two were treated with mist. alba (purge) and daily enemata. They were discharged after thirteen and fifteen days' treatment. Two were given mist. alba and an extra ration of meat. They were fit for discharge in twelve days and returned to duty.

The ambulatory cases.—Two men had been classified with the ambulatory subjects, who had all been put on the calcium and purge therapy but they did not show any improvement. It was considered that admission to the hospital was the best for them but, at that time, new rice came to hand and was issued to the men. Within five days these two subjects cleared up completely without recourse to admission. No cases terminated fatally in this epidemic.

Whether the lines of treatment follow calcium therapy or purgatives, it is considered that the therapeutic measures adopted against this disease must necessarily be entirely palliative. Not for one moment is it maintained that these measures can ever effectively compete with the simple expedient of altering the dietary to exclude deteriorated rice. In short I am strongly of the opinion that this is the crux of the entire condition. Granted that the disease, especially in the prison, can be effectively treated, the advocacy of prevention, is, I consider, the solution of the problem.

POST-MORTEM FINDINGS

Twenty-four cases were examined after death at Kissy Asylum and one at Connaught Hospital. They were almost all of a stereotyped nature, with oedema of the limbs, pericarditis with effusion and absence of nephritis. In detail, the necropsy in these cases gave the following results.

Externally, oedema, although constantly present in the legs, was elsewhere variable. Some cases had ascites and three had oedema of the face and neck. In some the abdomen was collapsed, in others distended with gas and ascitic fluid. Cutting into the oedematous subcutaneous tissues and muscles showed them to be sodden with serous exudate. The pleural sac contained variable amounts of clear serous fluid, varying in volume from two to twelve ounces. The lungs were adherent to the pleura, chiefly behind and some localized adherent patches were present anteriorly and at the mid-lateral right side (near the apex of the middle lobe). The lungs, themselves, in all cases were oedematous. The pericardium in all the subjects contained clear, free, serous fluid of straw colour. No bile staining, blood cells or blood staining was present in the fluids examined. The volume in the pericardial sac was variable from three to eighteen ounces. The heart showed great hypertrophy in all directions and the right auricle and ventricle were constantly dilated and filled with blood and a small amount of white ante-mortem clot. In all the cases, the valves were competent and revealed no vegetations or other signs of chronic impairment and there were no signs of endocarditis or aortitis. The heart muscle generally was considerably thickened and hypertrophic, without fatty degeneration or infiltration, but showing separation of its muscle fibres by oedema. Except when death had recently occurred, and where necropsy was performed in less than nine hours after death, the abdomen was distended with gas. In the peritoneal cavity of all cases free serous fluid was present varying in amount from a few ounces to two pints. All the cases showed 'pseudo-bile' staining of the abdominal fat. On examination this colour change proved to be due, not to haemolytic products, but to palm oil and no bile reaction could be obtained from this tissue. The distension of stomach and intestine was of variable amount and this was probably due to decomposition processes with gas formation. At the duodenum was found constantly areas of engorged tissues, with, in three cases, evidence of ankylostomiasis.

The mucosa of the stomach and upper part of the small intestine generally revealed this same type of engorgement and, in three subjects, petechial hæmorrhage of the duodenum was added to the hyperæmia. The liver was constantly but slightly enlarged and œdematous and showed evidence of venous congestion. In every autopsy the gallbladder was distended, smooth, glistening and of a dark green colour. There were no signs of adhesions and the surface of the gallbladder did not show the characteristic honeycomb markings of beriberi avitaminosis as described by Tull. The spleen was enlarged on an average to one inch below the costal margin and it was œdematous. The kidneys were of normal size, pale and œdematous, with normal capsule. There was no evidence of nephritis. The suprarenal bodies in five cases were somewhat enlarged and one contained evidence of infarction. No gross changes were observed in the nervous tissues, the bones or the pancreas.

Rice analysis.—The analyses of the rice for general purposes were estimations of carbohydrate, protein, fat, water, ash, cellulose, phosphorus and amino-soluble nitrogen. They were conducted along the well-known standard methods.

Chemical analysis.—The analysis of the rice, with special reference to the husk, was not deemed necessary for inclusion in this report because in the milling this article is a waste product and is not used for eating purposes. Attention was directed chiefly to the rice grain and the pericarp, with special emphasis on the type of rice which was known to produce the disease, when fed to human beings.

The colony's new season's rice was employed at first as a standard for comparison of the protein, carbohydrate and fat content and caloric value, but it was suspected that these values would not shed much light on the causal factor of the disease and, in the light of biochemical work done on the decomposition products of the protein layers, I feel sure that the general analysis of the food-stuff, although interesting, is not of paramount importance.

Beriberi standards.—Among the conclusions of Vedder and Feliciano (Philippine Islands experiments) are to be found chemical standards for estimating the anti-neuritic (anti-beriberi) value of a rice in the absence of any direct method of obtaining the exact amount of anti-beriberi vitamin. These standards include:

(a) Any rice having 1.77 per cent P_2O_5 plus fat, but not less than 0.4 per cent P_2O_5 .

(b) Any rice not having less than 0.5 per cent P_2O_5 with at least 75 per cent of the external layers of the grain.

Sierra Leone rice comes well up to these standards with:

(a) P_2O_5 —0.57 per cent plus fat $1.84 = 2.41$ per cent.
(b) P_2O_5 $\quad \quad \quad = 0.57$ per cent.

and, according to their accepted theories, there is little risk of development of true beriberi, when the staple diet consists of this colony's rice. The rice has a high anti-neuritic value, is well balanced in terms of protein, carbohydrate, and fat and has an energy value of sixteen hundred and fifty calories per pound.

Diseased rice.—The chemical work was chiefly directed against the 'faulty' rice, which, from observations at Freetown Prison and Wilberforce Barracks, was known to be associated with the œdema. When this rice was replaced by new season's rice or was specially treated in cooking, the œdema subsided and no new cases appeared. This rice was supplied as husk rice (paddy) and milled in the usual way before distribution to the various consumers. In this substance attention was particularly directed to the end-products, namely, the rice and the pericarp dust, both of which were submitted to chemical analysis in the usual way, the husk, as before, being discarded.

Fungoid rice polished 40 per cent pericarp

	Percentage
Carbohydrate	77.24
Cellulose	0.74
Fat	0.46
Protein	8.46
Water	12.32
Ash	0.78
P_2O_5	0.21
Soluble nitrogen	0.25

The faulty rice was milled and partly polished (40 per cent pericarp). The odour was slightly musty. Mycelial hyphæ and spores were seen on the surface of the grains. It was a mixture of white and discoloured grains (yellow, brown, black) up to forty per cent. Evidence of weevil activity was noticed in the bored grain, and weevils themselves (identified as *Calandra oryzae*, *Calandra granaria*, *Tribolium ferrugineum* and *Silvanus advena*) being present together with rice bugs and maggots. Fully thirty-two per cent of the grain was bored and showed evidence of larvæ. The rice had a relatively high percentage of broken grains, amounting to thirty-seven per cent. On an average, the amount of germ was low, nine per cent of the grains had all the germ, forty-four per cent contained a portion and in the remainder the germ had been completely removed either by milling or by parasite activity. The presence of fungoid grain was noted and especially in the discoloured grain could be seen mycelial threads, which were not so common on the sound white grains.

There is at once apparent a deviation from the standard rice in terms of fat, P_2O_5 and amino-soluble nitrogen; the other constituents being practically unaltered. The combined deviation was thought to be due to parasite activity in the old rice. With this aspect in view, considerable attention was given to the diseased rice products and later to the pharmacological action on animals of extracts of this rice.

Diseased rice polishings.—The pericarp dust was subjected to the same type of analysis. This dust is slightly acid in reaction, musty to smell and, when inhaled, causes violent sneezing and coughing. The prisoners employed in the mill are given expectorant cough mixture at the end of each shift to relieve the sensation of oppression it causes, which is worse when the old rice is milled. Some of the men appeared to develop asthmatical attacks when they went on the job at first and in the morning when work commenced. The dust floating about from the mill does not contain free sand in any large volume, even at the outlet of the machines, and it does not cause silicosis; examination of sputa for this condition was entirely negative for the presence of sand and *B. tuberculosis*, although vegetable fibres are quite commonly embedded in and lying upon large desquamated macrophage cells from the pulmonary epithelium. This pericarp dust was subjected to the same type of analysis before which it was entirely freed from sand and from a large amount of adventitious cellulose fibre derived from the husk.

Certain aspects are immediately obvious; the increased water content, always generally associated with fungoid activity, together with the diminution of fat and phosphorus and the big increase in the soluble nitrogen into the nature of which obviously it appeared enquiry may be made with profit.

Effect of washing rice.—Before proceeding to submit the work done on extracts of the faulty rice and of the pericarp, it is considered advisable at this point to state the effect on the grain of washing. From now onward, unless otherwise stated, it will be understood that the rice mentioned is the deteriorated grain, which was known from experience to be faulty and to produce œdema when eaten and the terms bad and faulty rice will be discontinued.

(a) **Rice.**—Apart from removing sand, adventitious insects, weevils, and dust, washing with water has a definite effect on the rice itself. The grain is washed

in cold (85°F.) running water for ten minutes, as the equivalent of the native method in which the washing is done in large pans with several changes of water. Thereafter, the grain is sun-dried and analysed in the usual way. The analyses are tabulated below:

	Before washing Per cent	After washing Per cent
Carbohydrate ..	77.24	76.97
Cellulose ..	0.71	0.71
Protein ..	8.46	8.18
Fat ..	0.46	0.46
Water ..	12.32	12.89
Ash ..	0.78	0.76
P ₂ O ₅ ..	0.21	0.18
Soluble nitrogen ..	0.25	0.16

Very little change takes place in the nutritional aspect as expressed by the calorie value. Carbohydrate, fat and protein are more or less the same, but there is a definite, but slight, loss in the phosphorus estimate, amounting to 14.28 per cent. I consider, however, that apart from obvious impurities soluble toxins, expressed in terms of soluble nitrogen, are definitely lessened by the washing. Although the soluble nitrogen quota is reduced considerably from 0.25 per cent to 0.16 per cent, it is apparent that an appreciable amount remains, even after the thirty-six per cent loss. The phosphorus loss has been considered a loss in terms of vitamin B. McCarrison and Norris proved that any rice originally shown to be beriberi-preventing may, with removal of a large percentage of P₂O₅ by prolonged washing, be altered into a "non-beriberi" rice, but, although this holds for .. it does not do so for the edema under consideration, where the vitamin B content is more than adequate. Some other causal agency was held to be at work.

(b) *Pericarp*.—Results of a similar nature were obtained with pericarp dust. The rice polishings were washed in cold running water for ten minutes, squeezed dry, spread out in the sun and dried for two days. As in the case of the rice, no form of artificial heat or of desiccation was employed.

Fungoid pericarp dust

	Before washing Per cent	Sun-dried. After washing Per cent
Carbohydrate ..	48.18	48.92
Cellulose ..	3.68	3.66
Protein ..	11.21	10.98
Fat ..	14.74	14.70
Ash ..	8.33	7.02
Water ..	13.86	14.72
P ₂ O ₅ ..	3.61	2.48
Soluble nitrogen ..	0.44	0.29

The results are similar to those obtained after treating rice with water. Washing does not affect, to any appreciable degree, the value of protein, carbohydrate or fat, but the main influence is shown in the soluble nitrogen and phosphorus content. In the former there is a reduction of 34.09 per cent and in the phosphorus value washing lowers the content by 31.30 per cent.

Washing with hot water.—The influence of washing was studied in terms of cooking. The rice is brought to boiling point and the rice water decanted and rejected. It is equivalent to considering that the rice undergoes part of the normal cooking process when it is washed in boiling water.

Two experiments were made:

(a) in which the rice was thrown into boiling water;

(b) in which the rice was put in cold water and heated to boiling point.

In both, after boiling had continued for three minutes, the water was decanted and strained off and the rice dried in the sun for two days. The usual analyses were made on this final dry rice product.

	(a) Boiling water Per cent	(b) Cold water to boiling Per cent	Unboiled and unwashed
Carbohydrate ..	75.53	72.65	77.24
Cellulose ..	0.62	0.60	0.74
Protein ..	7.88	6.46	8.46
Fat ..	0.34	0.22	0.46
Water ..	16.93	19.47	12.32
Ash ..	0.70	0.60	0.78
P ₂ O ₅ ..	0.14	0.12	0.21
Soluble nitrogen ..	0.02	0.00	0.25

It is obvious again that, with special reference to all the proximate principles, the energy value of the rice is not seriously impaired by this treatment, when it has been boiled and the rice water rejected. This value is, undoubtedly, not so greatly affected by throwing the rice into boiling water for a few minutes, as when the rice is brought slowly to boiling point, because then the degree of imbibition of water is less with correspondingly higher value of protein, carbohydrate and fat.

By either method, although the loss is fairly considerable (33.3 per cent and 42 per cent), the phosphorus element is not by any means all removed by short immersion in boiling water. Soluble nitrogen, however, shows results which are to be expected from the method of its estimation. The reduction amounts to 92 per cent of the total original soluble nitrogen method (a) and to complete absence in (b) when the rice water is brought to boiling point 'from the cold'.

Results of a similar nature were obtained by extracting the pericarp dust employing these same methods; that is, a large reduction in the P₂O₅ content and in the soluble nitrogen. However, as this is a waste product, it is not deemed essential to submit the results.

For the purpose of this research the intimate analyses of the rice washings are not given here, as this aspect is more or less of academic interest.

Culture of grains.—Inspection of the rice revealed, as was mentioned above, the presence of discoloured grains, mixed with normal white rice. These grains were divided into two groups, yellow and black, for culture experiments and special analysis. The discoloured grains were, in all cases, found to be dead; microscopically, erosion of the starch was in progress and the grains were contaminated with mycelial septate filaments. Samples of white, yellow and black grains were surface sterilized and put in a warm moist chamber for thirty-two days. All the rice samples increased in water content. The black grain became sodden and soft. Its soluble nitrogen content increased from 0.59 per cent to 0.85 per cent, with very slight loss in the P₂O₅ due to imbibition of water by the grain. The yellow grain turned to a dark brown colour, almost black, absorbed water but it did not become sodden and soft like the black variety. The soluble nitrogen increased also in this case from 0.28 per cent to 0.39 per cent, again with slight alteration in P₂O₅. The white grain, like the other two groups, developed a heavy growth of mould, but the colour change was not so marked. Some of the grain (3 per cent) became brown and some (35 per cent) was stained yellow, but the rest was more or less unaltered in colour, being, if anything, of a greyish tint. The soluble nitrogen increased in this sample, as in the others, from 0.03 per cent to 0.09 per cent. It was assumed that these conditions, although not by any means similar to normal storage, would reproduce rapidly in the grain that which occurs in storage in the country over a long period of time. Under conditions of moist warmth, with the possibility of increased temperature by fermentative processes in a large mass of grain, heat is generated and cannot escape readily from the decomposing mass. In this way, with heat and humidity, the growth of fungi and of other organisms is exceptionally rapid, with the net outcome that decomposition proceeds apace.

Preliminary work with extracts.—The first extracts made of the rice were evaporated *in vacuo* to small bulk without attention to percentage concentration. They were sterilized, without heating, and injected subcutaneously into normal subjects, and to oedematous cases. Localized oedema resulted, associated with a marked reaction. Similar extracts were scratched into the skin and there was produced a flat raised wheal with white centre due to vasoconstriction together with a surrounding zone of slight erythema, such as is obtained when histamine and allied substances are injected intradermally. Subsequently from the rice polishings, both unfermented and fermented, raw and cooked, extracts were made and tested chemically and biologically.

Chemical assay of extracts.—The reactions were suggestive of the histamine group of substances, obviously, therefore, the chemical tests, in view of these reactions, were directed to a study of the iminazole derivatives in the extracts, and one of the most delicate chemical tests for this group was employed. The rose-pink colour struck by alkaline sodium diazobenzene-sulphonate is given by dilutions of histamine even to 1:10,000 but this reaction is not, however, absolutely characteristic of histamine alone. It may be given by any iminazole derivative containing a free amino group, together with a replaceable group in one of the two, four or five positions, with the exception that no colour is given should a nitro-carboxyalkyl or carboxyanilide group occupy the four or five positions and it may be obtained in the presence of bases in the arginine, purine and tyrosine groups. A negative result is taken to show that histamine is absent, or, if present, only in infinitesimal quantities, but a positive reaction shows that either it or the allied bases may be present. The most reliable test is obtained by biological assay, employing intradermal tests and the effect of the substance on the isolated uterus, together with the persistence of these effects after alkali hydrolysis.

Extracts of rice.—The extracting media employed were all found to give negative results when used as controls, either chemically or biologically, and the same weight (100 grams) of material was used from which the extracts were made, together with constant volumes of the various extracting agents.

All the extracts made from new rice gave entirely negative reactions to the histamine intradermal tests. Similar results were obtained from rice that had been—

(a) put in cold water and heated to boiling;

(b) immersed for a few minutes in boiling water.

Dry faulty rice, however, gave positive results in most cases. In the presence of increased proportions of discoloured grain, the reactions were increased in intensity. The polishings from the faulty rice yielded reactions of a very definite type. It was, however, when employing the mouldy grain and fermented pericarp dust that the strongest effects were obtained, especially from rice with a high percentage of black mouldy grain showing putrefactive changes.

There was obtained a definite increase in these histamine bodies when the discoloured grains were kept for a period in the warm moist chamber. The intensity of the reactions was greatest with black grain, less with yellow and from the white rice no reaction could be obtained.

Feeding experiments.—Feeding experiments were conducted at Connaught Hospital and at Wilberforce, employing fowls and guinea-pigs. In the earlier observations, four fowls were used. Two were fed on washed [method (b)] grain and two had unwashed rice. These experimental animals were allowed to roam about as they pleased and to eat such green material as they thought fit. After five weeks, one of the latter died and was found to have congested liver and pericarditis with effusion. The lungs were slightly engorged. Its partner on the unwashed diet was killed one week later and found to have slight pericardial effusion with engorged crop and hyperæmia of the stomach and upper intestine. At the same time the other pair on the

washed rice were killed and found to be perfectly healthy.

Guinea-pigs were useless for feeding with dry material because they refused flatly to eat the rice. This was, to a large extent, overcome by making an extract of the grain, mixing this into bread and feeding the wet product to the animals which ate the mass avidly. The animals thrived on the extract from standard rice and from musty rice which had been washed. When killed the carcasses were those of healthy animals.

Extracts from dry, faulty rice and pericarp did not kill the animals immediately but they went off their food after fifteen days and refused to take the quantity they consumed at first. One animal died after twenty-one days on this food (bread soaked in aqueous extract of rice). It was found to have slight oedema of the lungs and acute gastro-enteritis. Three guinea-pigs were fed with greens, grass (their usual food) and with the addition of bread soaked in an extract from the fermented discoloured rice grains. Ten days later the first animal died; its two companions succumbed the next day. The post-mortem examinations again showed oedema of the lungs with gastro-enteritis, engorged intestine and hæmorrhages at the upper area of the duodenum. These animals apparently suffered intense pain, as they were exceptionally tender to touch, listless and breathless. They became very weak and scarcely had the energy to run away when approached.

Inoculation.—To ensure absence of bacteria and yeast spores, the extracts were freshly made and sterilized, without heat, which might have altered the toxins. Guinea-pigs were used into whose flanks the extracts were given subcutaneously only.

The extracts of new season's rice caused no sickness in the experimental animals. No ulcers or abscesses were produced at the site of inoculation. The animals were injected daily for eight days and found to be normal when killed.

Inoculation of sterile extracts of the old fungoid rice made the animals highly excitable five minutes after injection but in half an hour this passed off. Three days after inoculation commenced the animals became listless and refused to take their food. Of the three animals used, two died after five days of injection treatment (an injection of one c.c.m. extract being given daily) and the remaining one died in seven days. All showed similar pathological changes. Around the sites of injections were zones of hyperæmia but no pus or septic condition was observed. The heart was congested, the lungs engorged and distended with blood, and there were punctate hæmorrhages in the small intestine.

An extract made of pericarp dust that had been kept under moist conditions was sterilized and inoculated. This animal died one half hour after. Autopsy revealed hyperæmia around the site of inoculation. The lungs were fully distended but not oedematous. The right heart was dilated, the intestine gorged and the stomach in spasm. Entirely negative results were obtained from the injection of sterile extracts of washed rice.

The contraction of the isolated involuntary muscle was studied in a roughly constructed piece of apparatus, using preparations of the uterus and intestinal muscle of the guinea-pig. The preparation passed into powerful contraction on exposure to an extract of the faulty pericarp dust. This contraction was not, in any way, counteracted by the addition of atropine.

Urine analysis from patients.—With the exception of two suspected cases of oedema in whose urine was found albumin with granular casts, no obvious pathological changes of the usual types were found.

The urine in general was pale straw-coloured, very slightly acid, having a specific gravity of 1022. When passed, it was free from sediment and mucus clouding but, on standing till cold, earthy phosphates were deposited. The usual ammoniacal phosphates appeared on allowing it to stand for twenty-four hours. In almost all the cases the output of an excessive amount

of the earthy phosphates was commented upon and considered, to be not clinically normal. The buffer action of phosphate in the blood is considerably higher than that of sodium bicarbonate, from which observation it is suggested that the increased urinary phosphate value represents the end-product of a successful attempt by the alkali reserve to neutralize the acidity produced in the toxæmia. The absence of albumin and the presence of these phosphates tend to show that the renal mechanism in this disease is not grossly abnormal; an observation confirmed at the post-mortem findings.

Only in the severe cases was the indoxyl reaction obtained to a marked degree but almost all the specimens of urine from the patients gave a positive test indicative of indole b. acetic acid. Albumin, blood sugar, diacetic acid, acetone bodies and bile products were not observed to be present in pathological amounts in these urines.

Fæces analysis.—Apart from the presence of a trace of occult blood in seven cases, the analysis of the fæces did not shed light on the problem.

Blood calcium.—The recognized methods of analysing the amount of calcium in the blood were employed in a study of some of the prison cases. On an average, the results showed calcium deficiency (7.6 mg. per 100 c.cm.) which is a definite deviation from the accepted normal value of 10 mg. per 100 c.cm. The work along these lines continues.

In the main, I have submitted the results of the observations and findings from the biological aspect of the research, without, in any way, attempting to give every detail of the technique employed, which followed generally the standard methods in use.

DISCUSSION OF THE PROBLEM

The disease most commonly puts in an appearance when old and new rice crops have been mixed and Mr. Biddle has noticed that the disease breaks out in the year succeeding that of a bumper crop, with large stocks of old rice left in the dealer's hands after the new crop comes in. The new crop contains a much greater proportion of moisture. In these circumstances, mixing appears to favour decomposition. Fungi and the dormant spores of fungi have improved facilities for growth on account of the increased moisture content of the mixed mass and of the heat engendered, as in some cases of so-called spontaneous combustion by the fermentative changes in a moist heap. Storage during a rainy season appears to be ideal for such organismal activity because of the heat and the high relative humidity. These, it is maintained, are the attributes that make the problem serious in this colony. It is held that the rice becomes highly toxic if it is a mixture of old and new crops and is stored in conditions that encourage destructive attacks by fungoid and other organisms. If mixing of crops is permitted there is absolutely no guarantee but that these outbreaks of fatal epidemic dropsy will be repeated and I make bold to assert that this is one of the essential factors determining the control of disease. In addition to the effect of mixing old and new crops, there is accumulating evidence that similar and rapid destruction occurs when new season's crop is kept in wet storage, or stored in an imperfectly dried condition. It has been observed, as in other tropical and sub-tropical countries, that the disease appears when grain is eaten after prolonged storage under moist warm conditions.

That there are changes in the intimate chemical structure of the rice is seen from the change in soluble nitrogen and phosphorus content. These are associated with putrefactive changes. With an increasing value in the soluble nitrogen content, there is found evidence of increasing destructive changes. That the destructive change results in the production of soluble toxic substances has, I think, been established clinically, biochemically and physiologically, when extracts of this rice are made and utilized either for animal inoculation or for chemical study. Apart from the observations made on human subjects and in the field of clinical

medicine, there are the concomitant results of the biological experimentation of which recapitulation is unnecessary. The toxic element is soluble in water, a point demonstrated by the beneficial effects of washing the rice and rejecting the rice water resulting in the almost entire removal of a soluble toxin whose nature is, essentially, that of the histamine-tyramine groups. It has been shown that the soluble nitrogen factor in relation to total nitrogen may be considered a reasonably good index of the toxicity of the food-stuff.

When new rice is given to patients suffering from the œdema under review, the disease rapidly clears. In a way this may be the outcome of several factors. There is the resistant state of the living rice germ to disease, associated with the non-destruction of the protein aleurone layer and there is the factor of time, as new season's rice has not been subjected to prolonged bacterial and fungoid activity. Consequently, one expects even from this last aspect little, if any, putrefactive changes.

When considered purely as a disease due to the lack of vitamin B, it is difficult to understand why, with the superabundant diet issued at the Freetown Prison, beriberi should continue to be present, and also, if its nature is essentially one of 'avitaminosis', why the disease should be of so protracted a type, when additional accessory food substances almost to excess are exhibited. On the other hand, the aspect that this disease of œdema is due to toxic absorption, finds support on a number of points.

Conclusion

œdema at the Freetown Prison, Wilberforce Barracks, and Kissy Asylum is not that of beriberi (avitaminosis) but it is akin to epidemic dropsy. It is not associated with any lack of or diminution of accessory food substances, as vitamin 'B', which has been supplied in copious amounts to the inmates of these institutions, nor is it allied with protein starvation. The disease is essentially one of auto-intoxication, due to absorption of highly poisonous nitrogenous putrefactive products, engendered in old rice by the activity of organisms acting in hot and moist conditions and producing bodies of a nature allied to the histamine-tyramine groups. The toxic substances are water soluble, especially in hot water, and they are capable of withstanding boiling water, without considerable alteration of their poisonous principles. This last observation is important, as recommendations have been made in former epidemics that the rice water should be saved and added to the soup.

The disease-producing grain has a musty odour and, generally with discoloration, displays the presence of decomposition and of fungoid activity. Consumption of such food-stuffs is fraught with great danger, resulting, *inter alia*, in the rapid onset of œdema of an extremely fatal nature.

Rice forms the staple food of the colony and owing to a rapid extension of swamp-rice farming during the past three years an export trade in it is anticipated. œdema, therefore, becomes a matter of serious concern, especially, where it is known that apart from its incapacitating effects this condition is attended by a very high mortality among consumers of rice which has been permitted to become decomposed.

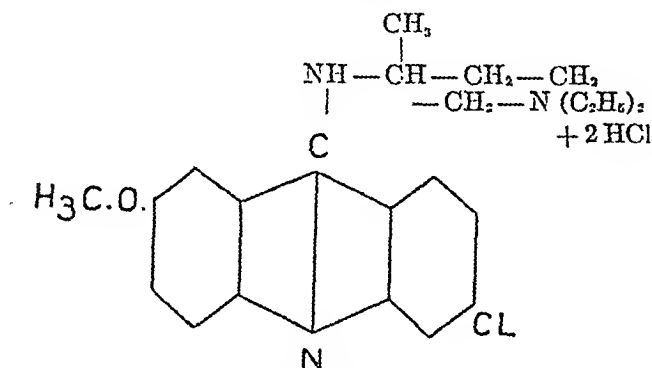
Correspondence

THE FORMULA OF ATEBRIN

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—The anti-malarial remedy Atebrin, which was synthesized in the scientific laboratories of Bayer-Meister Lucius, Elberfeld, by the chemists Mietzsch and Mauss under the direction of Professors Hoerlein and Schulemann has, according to information received from the said laboratories, the chemical composition

of 'Dichlorhydrate of 2 methoxy-6-chlor-9-alpha-diaethyl-amino-delta-methyl-pentyl-amino-acridin', and has the following constitutional formula:



Further details can be obtained from a paper by Mietzsch and Mauss in the *Klinische Wochenschrift* of 19th August, 1933.

Yours,
O. URCHS.

THE DOSAGE OF PLASMOCHIN

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR.—The importers of the French anti-malarial remedy Gametoxyl have lately issued an advertisement pamphlet giving a résumé of a paper by Dr. E. Charron, Paris, on anti-malarial preparations. The author compares at the end of his paper Plasmochin Compound with Gametoxyl, referring particularly to the time of treatment and the amount of medicament required for a complete anti-malarial treatment.

In his statement he mentions that the *daily* dose of Plasmochin Compound amounts to 12 to 16 tablets of the drug and that the total number of tablets required for a complete treatment lasting six weeks is 328 tablets.

Although the above dosage refers to our old, discarded tablets containing $\frac{1}{16}$ th grain Plasmochin and $\frac{1}{16}$ th grain quinine sulphate, this dosage would be decidedly dangerous, and we should be greatly obliged if you would issue a warning in your esteemed journal against using the dosage mentioned by this writer. Physicians are strongly advised to use only the dosage recommended in the authentic medical literature and the official pamphlets of our firm, who can only hold themselves responsible for the dosage recommended by them.

Thanking you in advance,
We beg to remain,

Sir,
Yours faithfully,
HAVERO TRADING CO., LTD.

15, CLIVE STREET,
CALCUTTA,
12th September, 1933.

SERVANTS OF INDIA SOCIETY FLOOD RELIEF FUND

To the Editor, THE INDIAN MEDICAL GAZETTE

DEAR SIR,—The heavy losses suffered by the people of Cuttack and Puri Districts owing to heavy floods and breaches in the several embankments in the said areas this month have called for sympathy from all quarters. Hundreds of homes have been swept away, thousands of people are now without shelter. Their agricultural lands have been mostly covered with sand. They are without much clothing. Immediate and instant relief will be needed for them. Government has also admitted this fact in their communique published from Ranchi on 16th August. About 40 by 50 square miles have been devastated.

I, therefore, appeal to you to help these distressed people through me. I am a public worker of that part

of the country and a life-member of the Servants of India Society. I have been doing this sort of relief work for the last 15 years in U. P., in Bengal and B. and O. I worked in Garhwal Famine Relief in 1918, in East Bengal Cyclone Relief in 1919, in Puri Famine Relief in 1920, in the Vaitarani Flood Relief in the Kconjhar State in 1927.

May I hope, therefore, that you will be pleased to entrust your charity to me.

Yours, etc.,
L. M. SAHU, M.A.,
Member.

SERVANTS OF INDIA SOCIETY,
CUTTACK,
30th August, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL A. J. H. RUSSELL, C.B.E., Officiating Deputy Director-General, Indian Medical Service, is confirmed in that appointment, with effect from the 28th July, 1933.

Lieutenant-Colonel C. Newton-Davis, M.C., Officer Commanding, Indian Military Hospital, Delhi, is appointed to officiate as Chief Medical Officer and Civil Surgeon, Delhi, in addition to his own duties, during the absence of Lieutenant-Colonel Wilson on leave.

Lieutenant-Colonel T. C. Boyd, on return from leave ex-India, has been re-appointed as Principal, Medical College, and Superintendent, Medical College Hospitals, Calcutta, with effect from the 6th August, 1933.

Lieutenant-Colonel K. S. Thakur, Civil Surgeon, Howrah, is appointed as Civil Surgeon, 24-Parganas, during the absence, on leave, of Lieutenant-Colonel A. Denham White.

The services of Lieutenant-Colonel J. Findlay are placed permanently at the disposal of the Government of Burma, with effect from the 3rd February, 1925, for employment in the Burma Jail Department.

The services of Major J. E. Ainsley are placed permanently at the disposal of the Government of the Central Provinces, with effect from the 17th August, 1933.

The services of Major A. J. D'Souza, M.C., late Senior Medical Officer, Port Blair, are replaced at the disposal of the Army Department, with effect from the 26th November, 1933.

The services of Captain J. C. Drummond are temporarily placed at the disposal of the Government of India, Army Department, with effect from the 26th August, 1933.

Captain A. Tait, Officiating Superintendent, Central Mental Hospital, Yeravda, was granted leave on average pay from 22nd July, 1933, to 22nd August, 1933 (both days inclusive). His services were replaced at the disposal of the Government of India, with effect from 23rd August, 1933.

The services of Captain H. S. Waters, Officiating Resident Medical Officer, St. George's Hospital, Bombay, have been replaced at the disposal of the Government of India, with effect from the 24th August, 1933.

The services of Captain A. M. Sheridan are placed temporarily at the disposal of the Chief Commissioner of Coorg for appointment as Civil Surgeon, Coorg, with effect from the 1st September, 1933.

To be Lieutenants (on probation), 1st August, 1933

F. W. Allinson, with seniority 1st August, 1932.
F. R. Cawthorn, with seniority 1st August, 1932.
F. V. Stonham.
J. F. J. Doyle.
J. M. Matthew.
W. B. Stiver.
J. J. Barton.
Leo Feinholts.

Original Articles

SOME COUNTRY BEERS OF INDIA

By R. N. CHOPRA, M.A., M.D. (Cantab.)

LIEUTENANT-COLONEL, I.M.S.

and

GURBAKSH SINGH CHOPRA, M.B., B.S.

School of Tropical Medicine, Calcutta

(Drug Addiction Inquiry, I. R. F. A. Series No. 18)

Introduction.—All races whether civilized or savage have made use of intoxicating drinks of some kind from time immemorial. Modern research has established the fact that alcoholic beverages were prepared from cereals by the Babylonians about 4,000 B.C. and ancient explorers have dilated upon the wonderful skill of man which enabled him to turn barley into wine. Primitive man in his progress towards civilization first developed the art of agriculture and there appears to be little doubt that the cultivation of barley preceded that of wheat. The use of these cereals in bread-making was intimately related to the manufacture of beer, and in ancient Egypt and Babylon bakers and brewers prepared bread and beer which were consumed by all classes of the community. Various kinds of beers were brewed in Egypt from different cereals and their use was intimately connected with the sacrificial rites performed in those days. The Egyptians taught the art of brewing to the Jews and Greeks, the latter transmitting their knowledge to the Romans. There is evidence to show that the Romans made ample use of this knowledge because beer was served to the armies of Julius Caesar as a ration. The beers of early days were flavoured with wormseed, ground-ivy, pine, willow-bark, etc.; hops only came into use very much later.

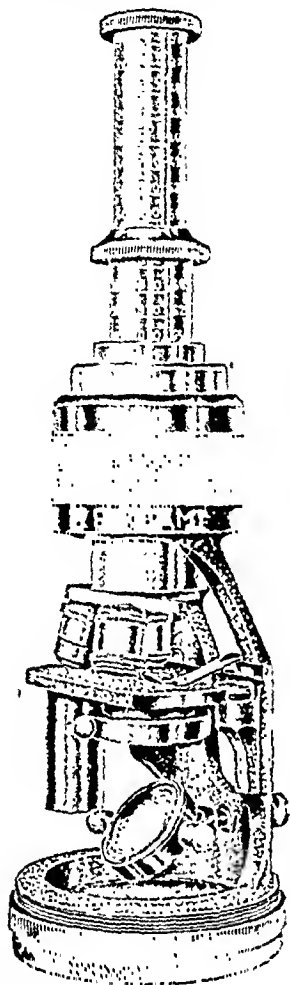
The ancient Aryan invaders of India were also well versed in the art of brewing drinks and earlier than 2,000 B.C. used a beverage called 'soma'. The exact nature of the 'soma' of the Vedic period is still wrapped in mystery and there are about a dozen different plants whose juice is said to have been the 'soma' so much talked about in Sanskrit literature. Hemp and ephedra figured in this list. According to Professor Max Muller 'soma' was probably a kind of fermented liquor. The 'soma' or 'homa' plant (*Sarcostemma* of botanists) was imported into India from the north by the Mongolian Tartar races. When properly squeezed it yielded a juice which was allowed to ferment and being mixed with honey it produced an exhilarating and intoxicating drink. According to Ray (1906) three kinds of liquors were known in the time of Manu, viz, *gauri* prepared from molasses, *madvi* from the sweet flowers of *Bassia latifolia* and *paishiti* from rice and barley cakes. Of these

paishiti was reckoned as the most common. The *suras* were included under the generic term *madya* meaning every kind of alcoholic drink. The word *kohala* occurs in Susruta a Sanskrit medical treatise written in the 5th century A.D., in which it means an alcoholic beverage made from powdered barley. Another word *jagala* also occurs in Susruta and in much earlier works such as Charaka, etc., in which *kohala* is not mentioned. *Jagala* was a kind of rice beer. It is probable that the English 'alcohol' and the Arabic 'aleohol' have the same origin as *kohala*. It would therefore appear that the art of fermenting starch and saccharine substances was understood and practised in India. The aboriginal races of India in all probability learnt the art of brewing from the Aryan invaders and from time immemorial they have been preparing and using such beverages. Some of these beverages are being used at the present time and in this paper we propose to give an account of the results of a survey of their incidence and the effects they produce.

Certain drinks and beverages commonly used in many parts of the Himalayas appear to be similar to those commonly used by Mongolian races. Some of these preparations resemble *shamshu* and *saki* used in China and Japan. The reason for this is not far to seek for the Mongolian stock gradually invaded India from the north-east, and evidence of this invasion still exists in the Mongolian characteristics of the Himalayan races at the present time. The use of such beverages in these parts is therefore easily understood and often they appear to form an important part of the dietary of the people. These liquors were also drunk by some of the aboriginal races driven southwards by the Aryan invaders, their use being essentially confined to the poorer classes. The materials used, the method of their preparation, and their general appearance, smell and taste are such as to be repulsive to the more refined races of Aryan stock, and among the latter only people belonging to the lowest ranks of society resort to these drinks.

Extent of use of Indian beers.—Our enquiries in the field show that country beers are drunk by Sonthals, Kols, Bhumijs, Bhutiyas, Mundas, Dosads and Oraons. The other tribes using these liquors are Haris, Bagdes, Domes, Moochis, Chandals, Jolas, Kaibartas, Mals and Dhangars. In the Darjeeling district, *marua* beer is universally drunk by Bhutiyas, Lupchas and other hill tribes. All the hill tribes in Assam, such as the Khasis, Lushis, Nagas, etc., use these beers as a common article of their dietary. The liquors are drunk equally both by males and females except that the Sonthal women sometimes object to the liquors as sold by licensed vendors and only take what is brewed at home. As far as our information goes no Hindus or Mohammedans of the higher classes take these beers.

sleeve enables the tube to be raised and lowered absolutely smoothly and uniformly, so that even with the highest magnifications the image remains perfectly steady. This also means great stability of the fine-adjustment mechanism, an important point when a microscope is in constant use.



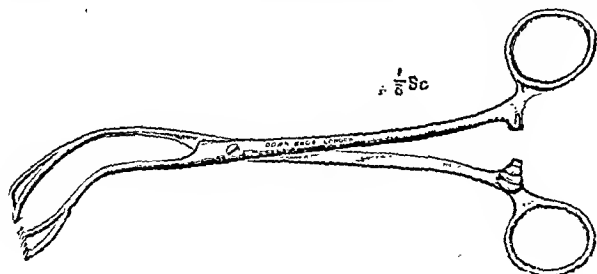
This novel microscope, owing to its small size (3 in. by 7 in.) and trifling weight (2½ lb.), should be peculiarly suitable for export.

The Hensoldt firm has appointed The Scientific Apparatus and Chemical Works, Ltd., Agra (U. P.), as their sole agents in India from whom the particulars and prices may be obtained.

TONSIL-HOLDING FORCEPS

By T. H. R. McKIERNAN, M.B., B.Ch.

THIS forceps illustrated herewith is nothing more than a modification of Duval's peritoneum pattern. The blades are curved to almost a right angle with the handle, so that when the tonsil is grasped there is ample room for the use of scissors or other instruments to carry out the enucleation. It has some advantages inasmuch that the tonsil is held firmly and may be drawn well out of the tonsillar fossa. No damage is



inflicted on the tonsil and the view of the operation field is not restricted. It is extremely light and in

practice it works well. It would be advisable to have a smaller size for use with children.

Messrs. Down Bros. have carried out my suggestions in making this instrument.

ADEXOLIN CAPSULES

EACH 3-minim capsule is precisely standardized to contain the vitamins A and D equivalent of 10 grams of high grade cod-liver oil. This preparation, which has been available to the medical profession since 1928, is valuable in the prophylaxis and treatment of infective processes, the high content of vitamin A serving to maintain the anatomical and functional integrity of the epithelial tissues, thus preventing the invasion of underlying tissues by pathogenic organisms, and the vitamin D reinforcing this 'anti-infective' action and at the same time maintaining an optimal concentration of calcium and phosphorus in the blood serum. The vitamin A is incorporated in the form of a special solution concentrated from the richest natural sources; the vitamin D is present in the form of the pure crystalline product (calciferol G. L.). The normal prophylactic dose for adults is one capsule a day—for example, during pregnancy, or for the prevention of such infective illnesses as influenza and the common cold. The dose for such treatment or for aborting infection may be much larger, up to a capsule every waking hour.

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indulge in polyandry. In the plains of the Punjab, Sindh, Rajputana and the western districts of the United Provinces beer is not used, its place being taken by such drugs as hemp preparations and opium.

Bengal and Bihar.—*Pachwai* is the universal drink of the aboriginal tribes such as Sonthals and Bhils inhabiting the Chota Nagpur hills which comprise the districts of Ranchi, Hazaribagh, one division of Bhagalpur and the Sonthal Parganas. In Patna, Gaya, Monghyr and Darbhanga, *tari* is largely used. On account of the migration of the inhabitants to the adjoining plain districts of Bengal, namely Burdwan, Birbhum, Bankura, Murshidabad, etc., the use of *pachwai* has spread all over this province especially in the western and northern districts which adjoin the Chota Nagpur hills and the Himalayas. In the northern and eastern parts of Bengal comprising the Darjeeling district, Sikkim and Bhutan borders, the use of a different kind of beer called *marua* is in vogue. In these districts home-brewing is permitted and, in addition, licences for retail sale are sold by auction to the highest bidder. Country beers are little used in Eastern Bengal, except in the two districts of Jalpaiguri and Malda.

Assam.—In Assam the consumption of beverages such as *zu*, *madh* and *laopani* is universal and they are the national beverages of the aboriginal hill tribes. They have also been adopted by some of the lower strata of Indian working classes such as the tea-garden coolies. Consumption of these beers is almost universal and extends along the border of the Himalayas right up to the Shan States in Burma. Little control appears to be exercised over their production in these areas. Further east there is the *marua* used in Sikkim and the neighbouring hills and *zu* used by the Nagas. Some of these tribes never drink water but always take these beers.

Central Provinces, Bombay and Southern India.—Similar beverages are also used in central and southern India in the hilly country stretching from Orissa to Godavari (non-regulated tracts of Madras Presidency). In larger portions of the Madras and Bombay Presidencies, the use of these fermented liquors has been replaced by *tari*. Here they are known under the names of *londa*, *henda* and *sonti soru*. The last named was formerly consumed by fishermen on the coast, but the grant of licences for its sale was stopped in 1897-98 because a more wholesome fermented liquor in the shape of toddy was available. Along the Western Ghats in the Bombay Presidency, there is evidence amongst the lower classes of some use of the beer called *boja* prepared from *mandwa*. The Indian Excise Committee (1905-06) however did not find any evidence of its present use there. Our observations in the field show that in certain hilly tracts of the Western Ghats *boja* is still used to

a small extent. Still further south a drink known as *akki bhoja* is largely used, particularly on the Mysore plateau in Milnad. The brewing and consumption of these liquors is subject to little or no control in the non-regulated tracts of the Madras Presidency.

In the following table the vernacular names of these beverages and the localities in which they are used are summarized:—

TABLE I

Vernacular names of beers and other liquors		Localities in which used
1.	<i>Sur, lugri, chang</i> and <i>arrack</i> are distilled from <i>mandwa</i> and rice beer.	Kangra district, Lahoul and Spiti valley in the Punjab and Kashmir.
2.	<i>Rabra, soma, pakhwai, boja, darbakra. Daru</i> (distilled liquor).	Jaunsar taluk of Dehra Dun district in U. P. Bhutya taluq of Kumaon division.
3.	<i>Pachwai, handia, marua, jaur, chanua, niger, kusha, sugda. Rakhsiki</i> (distilled liquor from rice).	In the western districts of Bengal, Bihar and Orissa, Bhutan, Sikkim and eastern parts of Nepal.
4.	<i>Madh, zu, laopani</i> ..	Assam, Nagas, Sadiya frontier tract and Tibeto-Burman tribes.
5.	<i>Boja, londa, sonti soru.</i> ..	Bombay, particularly Maharashtra in Madras.
6.	<i>Akki bhoja</i> ..	Mysore plateau.
7.	<i>Congec</i> ..	Used in Burma by Khyen and Karens.

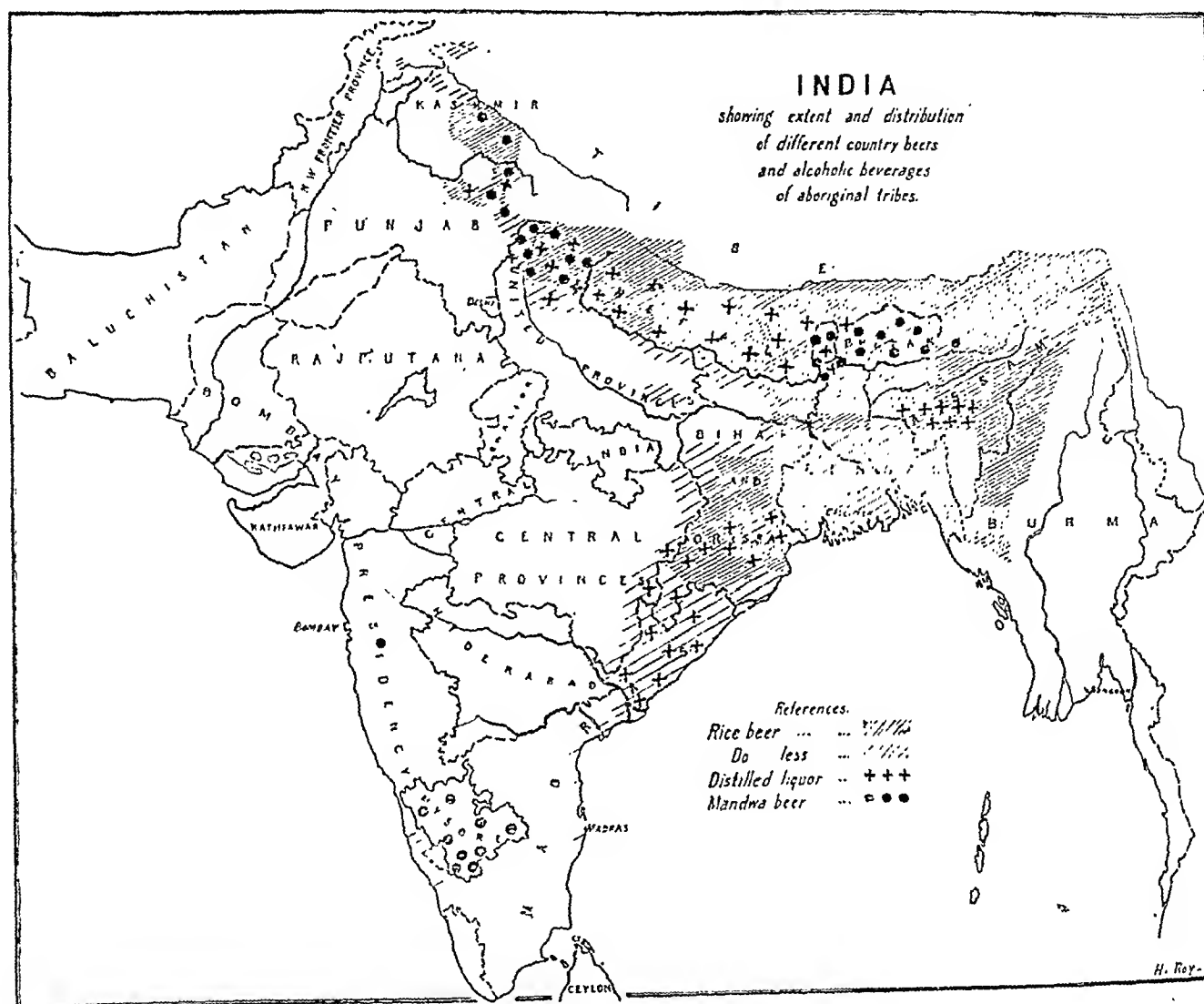
Methods of manufacture.—The two essentials for the manufacture of these beers are a fermenting material and a cereal to ferment:

1. **Fermenting material.**—This is generally supplied in the form of cakes of coarsely-ground corn permeated throughout with dry and empty mycelial filaments of mucus bearing numerous reproductive bodies in the form of chlamydo-spores. Besides, it also contains a certain proportion of the root tissue of a species of *Polygala* which secures in them the presence of a number of reproductive fungal elements capable of retaining their vitality for prolonged periods if they are kept dry. The proportion of *polygala* in the cakes has to be carefully regulated, as an undue proportion may lead to suppression of growth of the fungal elements. On the other hand any defect may fail to suppress the common and useless fructification of the fungus. It is interesting to observe how such difficult formulæ of the proper proportions of the various constituents of these cakes have been worked out by the uncivilized or semi-civilized tribes that resort to the use of these beers. These ferments are manufactured and sold throughout the whole length and breadth of the Himalayas and rarely they are even imported from Tibet, China and Central Asia. In places where the use of these drinks is very prevalent, the ferments are prepared locally under different names by certain tribes, the secret of their composition being carefully guarded. In their preparation a large number of essential elements are mixed

except in a few cases where Rajputs, Goalas, Kurin, Barhi, etc., whose economic condition is very low, have been found to resort to them.

Vizagapatam districts of Madras. In the attached map their distribution all over India is indicated :—

MAP.



In the report of the Indian Excise Committee (1905-06) the distribution of these beers is discussed in a general way and our observations made recently in the field show that the state of affairs has not changed very much since that time. Watt in his *Dictionary of the Economic Products of India* states that these beers are taken in certain tracts throughout India and that there is evidence of their past or present use as far west as Poona, and as far south as Canara and Mysore. They are not used very much, however, in the south where *tari* made from the coconut palm and stronger drinks such as *arrack* are more commonly used. These beers are also drunk throughout Bengal and Bihar with the exception of certain districts where *tari* made from the palmyra and date palms is used. They are also used in the United Provinces along the Himalayas from Azamgarh to Kangra district in the Punjab, and the non-regulated tracts of the Ganjam and

Northern India including the Punjab and the United Provinces.—In the United Provinces and the Punjab there is a small consumption chiefly in the Himalayas and the Tarai. The local names are *darbakra*, *soma*, *rabra* and *boja* in the former and *sur*, *lugri* and *chang* in the latter. The area along which these beverages are used covers the whole length of the Himalayas from Kashmir in the north to Lahoul, Spiti and Kangra. Beverages under the names of *chang* (of Spiti) and *lugri* (of Kulu) are both pernicious and foul-smelling drinks made from fermented rice. Home-brewing is allowed in certain areas under licence.

In Almora, Garhwal, the Jaunsar taluk of Dehra Dun district, Naini Tal and Azamgarh these beers are fairly largely used. In some of these districts home-brewing is allowed and in others their sale is allowed by licensed shops. In parts of Dehra Dun district these beers are drunk largely by certain Hindu races who

or four days when they are taken out, dried and subsequently kept dry, by storage near a fire-place.

The Luchas and Lushis as well as the Nagas make rice beer without adding any special ferment.

2. Cereals used and process of preparation :—

(a) *Pachwai* and *handia*.—These rice beers are the most extensively used of all the country beers. The process of manufacture is simple. Rice is boiled and spread on the clean floor or on a mat, mixed with finely powdered cakes of *bakhar* in proportion of 1 in 100, and left in an earthen vessel in a dark place to allow fermentation to progress. After four to ten days or longer, according to the temperature of the atmosphere and when the fermentation has fully progressed, it is taken out. The mass is then diluted with water which takes up all the alcohol formed and is drunk. The washings are repeated till the mass is bereft of all its alcoholic content and the rice is thrown away or given to pigs.

(b) *Sur* and *lugri* are similar beers prepared from fermented rice and sometimes from other cereals in Kangra district.

(c) *Zu* is a weak country beer which is the national drink of Angamai Nagas. It is prepared by pouring boiling water on rice and leaving the infusion for two or three days in a dark place by which time the fluid becomes fermented and is refreshing and exhilarating to drink. No special ferment to assist fermentation is said to be added in the process of its manufacture, enough ferment being present in the unwashed troughs to start the process.

(d) *Marua* beers (i.e., *chang*, *jaur*, *niger*, *chanua*).—These beers derive their names from a millet called *mandwa* (*Elusine caracana*) which is used in its manufacture. *Mandwa* forms the staple food in most of the hills. The grain is husked, boiled, cooled, and thoroughly mixed with the ferment *murcha*, two to four cakes being added to a maund (80 lbs.) of the boiled grain. The mass is then spread over the floor of a room to a depth of eight to ten inches and kept there from forty-two to forty-eight hours to allow the moulds to develop and spread throughout the mass. The whole mass is then transferred to bamboo baskets which are wrapped in plantain leaves, probably to prevent the introduction of extraneous organisms from the air. The grain is then allowed to remain in these baskets in a dark place for fifteen to twenty days, so that the organisms may produce the desired effect. After this period the grain is ready for use. Some of the prepared grain is placed in a vessel consisting of a bamboo cylinder known as *changa*; hot water is then poured into it and the mixture is left for a time. The liquor is then imbibed through a thin

reed or bamboo pipe. The vessel may be replenished repeatedly with hot water until all virtue is gone out of the grain. If an amount of water equal to that of the grain is added, the wash obtained is called *niger* but if twice the amount of water is added the resultant beverage is called *chanua*. The alcohol content of the liquor when used in this manner is very low (less than 1 per cent by volume), and men, women and children take a delight in sipping it from morning to evening. It is only when the fermented grain is kept steeped in an equal amount of water for twenty-four hours that the percentage of ethyl alcohol rises to six or eight per cent.

(e) *Pakhwai*, *rabra*, *daru*, *lugri*.—These are the common beverages in use in the western Himalayas and the Jaunsar Bewar Pargana of Dehra Dun district. They are prepared in a slightly different manner. A maund of the flour made from one of the common cereals, usually *mandwa*, is taken and made into thick cakes. These are crushed into small pieces and mixed with the ferment *kemki roti* and kept for four to five days in an earthen vessel having a capacity of about four maunds. Usually fermentation starts after this time. Then the vessel is filled with water and again kept in a cool place for about six to eight weeks to complete the fermentation. The resultant fluid is strained and is called *pakhwai*. The semi-solid material left behind is called *rabra*; it contains a certain amount of alcohol and is used as food.

(f) *Daru* or *mandwa* spirit.—This is a drink similar to the country spirit used in the plains. It is one of the choicest drinks of the inhabitants of Jaunsar Bewar and is used on ceremonial occasions such as New Year's day, Dewali, etc., and at marriage or other festivities. The method of preparation is as follows :—Eight seers of *mandwa* flour is baked into a single cake of about eight inches in diameter and one inch in thickness. It is broken into small pieces and mixed with the ferment *kemki roti* and eight seers of water is then added to make it into a homogeneous mass. It is then put into an earthen vessel and stirred twice or thrice daily and after one or two weeks the fermentation sets in. During the winter it may take three to four weeks before it is ready for distillation. The distillation apparatus and the method of its working are described in the diagram on the next page.

Rakhshi.—This is a distilled alcoholic drink used in the eastern portions of the Himalayas, particularly in Nepal and the adjoining areas. It is prepared by distilling the fermented beers used in those parts, e.g., *pachwai* and *marua*. Although distillation is not allowed under the law a large amount of illicit distillation goes on in the hills on the borders of Nepal. Besides this illicit distillation a country spirit called *rakhshi* made from rice is prepared and sold by

with a number of others which are not only unnecessary for fermenting processes, but as will be seen later are sometimes poisonous and extremely dangerous to health. The most important of them are described below :—

(a) *Bakhar*.—This is the most widely-used of all the ferment materials in the manufacture of the rice beers such as *pachwai*. It is stated in the report of the Bengal Excise Commission (1883-84) that 166 different plants and 45 different species have been used in its manufacture. We were able to collect many recipes from the *bakhar* manufacturers of Birbhum and Sonthal Parganas and we have found one hundred roots and 30 stems, leaves and flowers mentioned, which were said to be used in its manufacture. The list included poisons like *dhatura*, *aconite* and *nux vomica*. The commonest ingredient was a plant called 'Rannu' in Sonthali. Another common ingredient of the cakes is a plant known as 'Sarum Lutui' (*Clerodendron serratum*) which was especially used to enhance the intoxicating properties of the beer. In the northern Himalayas a grass, *Hardeum vulgare* Linn., is employed in the manufacture of these ferments. According to Ray (1906) the plants used in the preparation of *bakhar* may be divided broadly into four groups with regard to their known general properties :—

(1) Some possess medicinal properties, e.g., *Tribulus terrestris* (gokhur); *Desmodium gangeticum* (sálpán); *Uraria lagopodioides* (chakulia); *Splavum jacquini* (kantakari); *Hemidesmus indicus* (anantamul); *Asparagus racemosus* (satamuli), etc.

(2) Some contain bitter principles, e.g., *Andrographis paniculata* (kalmegh); *Oldenlandia herbacea* (khetpapra); *Azadirachta indica* (nim); *Justica adhatoda* (basak), etc.

(3) Some contain tannin, e.g., *Terminalia chebula* (haritaki); *Terminalia tomentosa* (piásil); *Cassia fistula* (sondal); *Diospyros tomentosa* (kendu), etc.

(4) Some contain narcotic principles, e.g., *Datura* (dhutura); *Plumbago zeylanica* (chita); *Strychnos nux vomica* (kuehila); *Cannabis sativa* (siddhi); *Aconitum palmatum* (bhikhma).

The first investigation of a scientific nature regarding *bakhar* was made by Ray (1906). He thinks that the saccharification of rice as well as the subsequent alcoholic fermentation are due to the activity of a micro-organism present in *bakhar* to which he gives the name *Mucor torula*. The next investigation on *bakhar* was made by Hutchinson and Ram Ayyar (1915). Contrary to the view expressed by Ray, they concluded that the changes were brought about by two distinct classes of micro-organism, namely, mucors and yeasts. Interesting observations were also recorded by these workers with regard to the relative physiological activities of the different micro-organisms

found in *bakhar*. A fungus named *Aspergillus oryzae* isolated from the Japanese koji, a substance analogous to the Indian *bakhar*, was found to possess the greatest saccharifying activity. Several specimens of *bakhar* were prepared in the Pusa laboratory by mixing pure cultures of *Aspergillus oryzae* and other mucors with yeasts and the comparative strengths of the alcohol produced by them from rice were recorded. Attempts were made by these workers to produce the crude *bakhar* from cultures of mucors and yeasts. *Aspergillus oryzae* a fungus isolated from the Japanese koji and several varieties of yeasts were utilized in the preparation of different types of *bakhar*. The results however were not satisfactory. The maximum strength of alcohol obtained by the action of these *bakhars* on rice was 33.7 per cent (59 per cent proof) against the maximum of 18.3 per cent (32 per cent proof) by volume, recorded with ordinary crude *bakhar*, thus showing that the product obtained experimentally in the laboratory was not identical with the crude product. Although the peculiar apple-like odour associated with the growth of *Aspergillus oryzae* was present, the taste of the *pachwai* prepared from the laboratory *bakhar* did not come up to the standard and liking of the consumers generally. *Mucor amylomyces* used in European distilleries is very similar to the organism found in *bakhar* and other fermenting substances used in the preparation of these beverages.

(b) *Kemki roti*.—This is the ferment used in Jaunsar and in the western Himalayas. Powdered and dried roots of several hill plants are mixed with four times their weight of *mandua* flour and made into a cake 2½ inches in thickness and 10 inches in diameter. The vernacular names of the plants used are *chhamur*, *artoo*, *mukrand pahar*, *baru*, *charwa* or *chharanta*, *doodth pal* and *sonti*. The mixture is then covered with straw and placed in a dark room for eight days or so, depending on the time of the year; after this it is taken out and dried in the open air for four days. The black fungal growth which occurs on its surface is wiped off, and it is then ready for use.

(c) *Murcha cakes*.—These are commonly employed in the eastern Himalayas, Assam and Bhutan hilly tracts. The outer skin of the roots of certain wild plants known as 'bhimsen-pati' (*Buddleia asiatica*), 'lour' and 'wadding-hang-ma' (*Polygala arillata* Ham.) are dried, powdered and mixed with other ingredients in the following proportions:—Dried roots 6 ounces, dried ginger 1 ounce, 6 chillies and rice flour 12 pounds. Sometimes one or two seeds of *Strychnos nux vomica* are added and the mass is then kneaded into a dough with water. Small round cakes are prepared and dusted over with an old powdered cake from a previously manufactured batch. They are then covered with fern leaves and kept in a dark room for three

and his results are given in the following table :—

Average strength of country beers (1905-06)

Province	Number of analyses done	Percentage of absolute alcohol by volume
Bengal	.. 8	6.4
Eastern Bengal	.. 4	6.9
United Provinces	.. 1	13.6
Punjab	.. 3	6.3
Burma	.. 7	9.9
Mysore	.. 1	4.1

In the following table the results of the analyses of similar specimens examined at the Municipal Health Laboratory, Darjeeling, during recent years are given :

TABLE II

Showing the results of the analyses of country beers done in the Municipal Health Laboratory, Darjeeling

No.	Specimen	Specific gravity	Percentage of ethyl alcohol by weight	Percentage of alcohol by volume
1	Undiluted pachwai, chanua.	0.9870	13.1	22.9
2	Undiluted pachwai, niger.	0.9981	10.68	18.7
3	Undiluted chanua.	0.9894	2.65	4.6
4	Diluted pachwai, niger.	0.9915	10.85	19.0
5	Do.	0.9803	4.33	7.6
6	Do.	0.9864	8.03	14.1
7	Chanua	0.9888	6.71	14.6
8	Do.	0.9968	1.8	4.0
9	Do.	0.9933	..	8.7
10	Do.	0.9945	..	6.8
11	Do.	0.9884	..	12.9
12	Do.	0.9915	..	10.8
13	Do.	0.9895	7.5	13.5
14	Do.	0.9903	7.09	12.4
15	Do.	0.9888	..	14.6
16	Do.	0.9932	..	8.29
17	Niger	0.9865	8.29	18.03
18	Do.	0.9944	3.1	7.0
19	Do.	0.9894	..	3.7
20	Do.	0.9930	..	8.75
21	Do.	0.9896	..	14.5
22	Do.	0.9894	..	13.7
23	Do.	0.9932	5.0	8.7
24	Do.	0.9822	14.18	24.8
25	Do.	0.9899	..	12.95
26	Do.	0.9876	..	16.4

A perusal of these results will show the large variations in the alcoholic contents of these beers. In three the strength of alcohol is very small, i.e., below 5 per cent, in seven it is between 5 to 10 per cent, in ten it is between 10 and 15 per cent, in four it is between 15 and 20 per cent, and in two it is between 20 and

25 per cent. It will be observed therefore that considerable quantities of alcohol could be consumed if these liquors were made stronger. Fortunately, however, in the majority of specimens the strength of alcohol is less than 15 per cent by volume, and this decreases the chances of drunkenness and noxious effects from this source.

Etiological factors.—These can be grouped under the following heads :

(1) Environmental and climatic factors. (2) Belief in medicinal value. (3) As foods and euphorics. (4) Religious, social and ethnological customs and beliefs.

An analysis of a large number of habitués examined by us shows that, with regard to the cause of their addiction, they can be roughly divided into two groups.

(a) Those who start early in life, i.e., before 30 years of age. Eighty per cent of the habitués started the use of these liquors before 30 years of age and in the majority of instances because of the prevalent belief regarding their tonic, exhilarating and nutritive properties. Association with and suggestion of their elders played an important part in their starting the use of these liquors.

(b) Those who start later in life, i.e., after 30 years of age. They comprise a small group some of whom took to these liquors because of their supposed beneficial effects in overcoming worry and fatigue, generally the result of hard work. Others took to them to promote appetite and digestion, and still others as a protective against the trying cold weather of the hills.

(1) *Environment and climate.*—In our series as many as 60 per cent admitted that they started these beverages from no other reason than the example of or association with their parents, relatives or friends. The parents sometimes, on account of the belief regarding their beneficial effects on health, give small quantities of the diluted liquors to their children. In cold and damp climates, particularly in the hills, large numbers of people start using these liquors as a protective against chest diseases, cough, etc., and finally they become habituated to them. The use of fermented liquors for similar reasons also prevails in areas of heavy rainfall, e.g., in the mountainous and sub-mountainous tracts of the Himalayas, Chota Nagpur hills and along the Western Ghats.

(2) *Belief in their medicinal value.*—When a relative or friend is feeling out of sorts or scedy usually a man habituated to these liquors suggests a dose as a curative. There is a strong belief amongst the inhabitants of these regions that these beverages are a necessity for everybody, as they keep out damp and cold and are a prophylactic against malaria.

(3) *As foods and general euphorics.*—Many of these beverages have a considerable food value. During the process of fermentation many indigestible carbohydrates are converted

contractors licensed by Government. This liquor is largely used by the Nepalese section of the population of the Darjeeling district and the higher-class Bhutyas residing there.

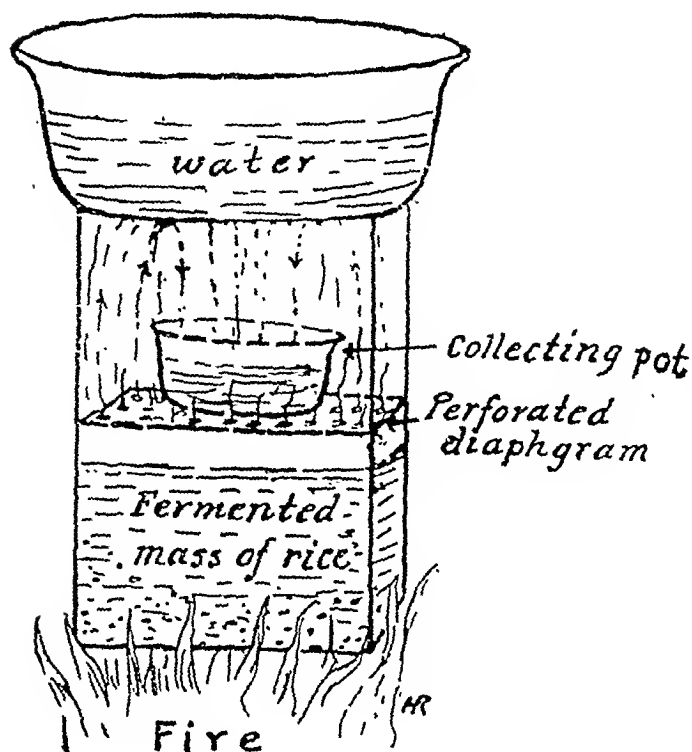


Diagram showing the apparatus and method of manufacturing rakshi (rice spirit)

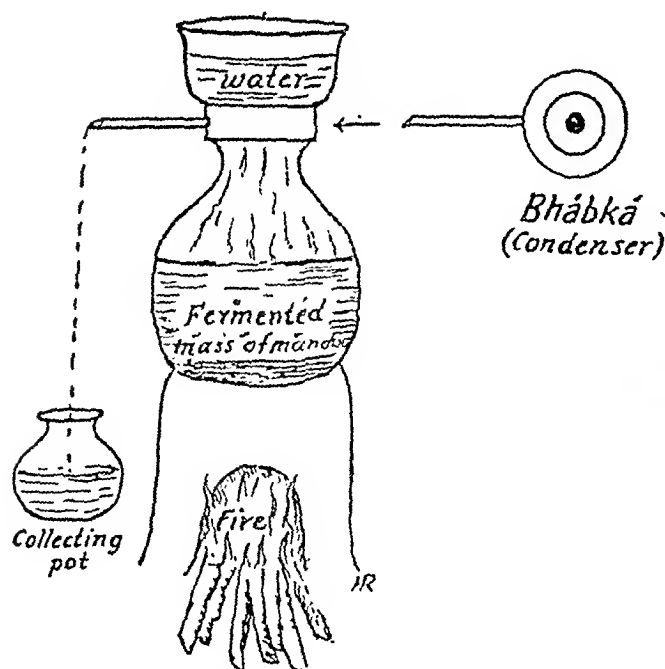


Diagram showing the apparatus and method of manufacturing mandwa spirit

(h) *Chang*.—This liquor is used in distilled or undistilled form in the hills towards Spiti, Lahoul and Kashmir.

Cereals used and composition of beers.—The cereals most commonly employed are rice and mandwa. The husked grains have the following composition :—

	Rice per cent	Mandwa per cent
Water	.. 12.8	13.2
Albuminoids	.. 7.3	7.3
Starch	.. 78.3	73.2
Oil	.. 0.6	1.5
Fibre	.. 0.4	2.5
Ash	.. 0.6	2.6

During the process of manufacture, starch is converted into sugar which later becomes converted into alcohol. These changes are brought about through the agency of various moulds and yeasts present in the fermentation cakes. Moulds such as *Rhizopus cambodja*, *Dematium* and *Penicillium* and one kind of yeast gain entrance into the fermentation cakes either from the skin and roots of the various plants used, or from the air or the green leaves used to cover the cakes during the process of their manufacture. The enzyme amylase secreted by these moulds changes the starchy matter into maltose which is then converted into glucose and ethyl alcohol by the activity of the maltose and zymase of yeast. Fermentation enzymes are also secreted by the moulds to a small extent.

Besides diluted ethyl alcohol, these liquors contain other starchy derivatives such as dextrine, malto-dextrine, maltose, etc., which have not been fermented. The food value of these liquors is therefore substantial. The nature of the by-products depends upon the character of the grain and the fermenting material used. In most of the fermented liquors glycerol is formed from decomposition of sugars by yeast; fusel oil is formed from amino-acids by the decomposition of proteins present in the grain; succinic, formic and acetic acids are produced and some other acids may be formed as a result of bacterial contamination. Besides these many esters, and aldehyde and ketone bodies, which are responsible for the smell and taste of these fluids, are formed.

Alcoholic strength.—The fermented mass has a semi-solid consistency and contains fair quantities of alcohol. The strength of the ultimate product depends partly upon the nature of the grain employed but much more upon the amount of water added to dilute it. The amount of water added varies in different places, amongst different tribes, and according to the occasion on which the liquors are used; for instance the liquor drunk at festivals and marriage ceremonies is much stronger than that used for daily consumption.

Bedford, at the instance of the Indian Excise Committee (1905-06), examined the alcoholic contents of a number of samples of rice beers collected in various parts of India

remainder six bottles and more. The number of those who drink excessive quantities and reach the stage of intoxication is small, certainly not more than 5 to 10 per cent even on Saturdays and Sundays, when the consumption is the highest. The plea used by advocates of these beers, namely that the quantity of the daily dose is moderate, is well borne out by our observations.

Sex incidence.—Unlike narcotic drugs in this country, these beverages are taken by members of both sexes alike. Forty per cent of the habitués in our series were females and among them there were many children of both sexes. The female habitués mostly take these liquors in moderate quantities as a mild euphoric and as food after a hard day's work or to keep off the cold. Women usually drink in their homes and we have very rarely seen them drinking in the licensed shops.

EFFECTS PRODUCED.

It may be emphasized here that the aboriginal races only drink fermented liquors and that the distilled liquors we have mentioned, e.g., *chang* from distillation of *mandwa* beer and *rakhshi* from rice beer, appear to be entirely an innovation brought by the Aryan races. In the following pages the effects of these beers and not of the distilled liquors are discussed.

There is a great deal of difference of opinion as to whether these liquors are wholesome or harmful stimulants. The effects produced by them are somewhat similar to those of ordinary malt beer. The immediate effects in habitual consumers are refreshing and stimulating. They alleviate fatigue and give rise to a sense of pleasure and general comfort (euphoria), accompanied by a feeling of vigour, and capacity for work. According to the habitués, these beers remove restlessness, induce forgetfulness and soothe the nerves. The drinkers are at first inclined to be silent but they soon begin to talk, become happy, courageous and even hilarious. They become sociable, the eyes brighten up and the usual depressing effects of alcohol on the higher centres become apparent. With larger doses the symptoms observed are similar to those met with after strong alcoholic drinks.

As regards the production of harmful effects our experience in the field is very much the same as that of the witnesses who appeared before the Indian Excise Committee. These liquors are not always innocuous and sustaining as is claimed by some people, and they undoubtedly lead to much waste of food material. Cases of excessive drinking have been reported and even deaths have been recorded in different areas after heavy indulgence. We have carefully studied the question of the fatal effects produced by the use of these liquors and have come to the conclusion that, even if inordinately large quantities are consumed, it would be difficult to take enough alcohol to produce stupor, coma

and death from drinking the ordinary rice or *mandwa* beers. Most of the cases of poisoning are undoubtedly due to drugging of these beverages. The allegation of drugging has been made in most of the provinces and, although in the case of spirits and *tari* evidence has been wanting, it has been obtained with regard to the country beers. In quite a number of the fatal cases, *dhatura*, *nux vomica* and *aconite* have been detected in sufficient amounts to produce death by over-indulgence in the beer containing them. All these poisonous substances have actually been detected in the fermenting cakes of *bakhar*. These drugs are surreptitiously added with the idea of giving the liquors a bitter taste and also of increasing their intoxicating effects.

Nutritive and digestive value of beers.—Beers generally are regarded as stimulating, refreshing and thirst-quenching beverages but doubts have been expressed regarding their food value. According to Bedford some of them contain 1.35 grammes of sugar and 0.65 gm. albuminoids per 100 c.cm. and some even contain larger quantities. There is no doubt therefore regarding their food value. In fact they have the combined value of food and stimulant. The quantities of carbon dioxide and other substances present may even promote digestion by stimulating various digestive juices and thus they may act as adjuncts in facilitating the digestion of other foods. They also supply quantities of salts of potassium and sodium, calcium phosphate, etc., which are among the more important of minerals required for the repair of the tissues after hard physical exertion. It is well known that plants of all kinds, including lower forms of vegetable growths, contain water-soluble substances which promote growth and nutrition. Brewer's yeast is a recognized source of vitamin. The crude beers which contain both these substances (moulds and yeasts) should therefore form very rich sources of growth-forming water-soluble vitamins belonging to the groups B₁ and B₂ and probably also vitamin C.

Most of these races are very poor and cannot always secure for themselves a varied diet containing all the principles required for proper nutrition. Our enquiries have convinced us that the majority of these tribes are subsisting on a poor, restricted and sometimes unbalanced diet of a monotonous character. It is remarkable however that these primitive people are peculiarly free from any of the deficiency diseases which have wrought havoc in several parts of the world from time to time. The beers have been shown to be rich sources of vitamins and it is not unlikely that the supply of vitamins through the agency of these beers is responsible for the lack of deficiency diseases in these communities. Yeasts also contain hæmatopoietic principles and have been used successfully in the treatment of anæmia.

into more readily assimilable sugars. The nutritive value of rice beers, such as *pachwai*, *zu*, etc., is undoubtedly substantial. The Nagas never drink milk or use milk as food. They always drink the rice beer, *zu*, prepared in their own homes. In the mountainous regions of India where economic conditions are poor and the natural craving for a stimulant is greater on account of climatic conditions, the use of a variety of beers and spirits, offered at prices commensurate with the means of the people, has come into vogue. These mild drinks are to the poor what the different varieties of expensive alcoholic liquors are to the well-to-do.

The habit of taking these beverages begins at a very early age. In some parts the children start small doses of the beers but this is an uncommon practice. Mostly, people resort to these drinks in order to tide over the feeling of exhaustion after a day's hard labour in the fields, in the tea gardens or during the trying winter season. *Pachwai* is used by practically all the male and female workers in the coal-mining districts of Bengal and Bihar, and they indulge in it after finishing their work which involves a considerable amount of physical strain. The doses taken are often moderate, just sufficient to relieve the feeling of fatigue and ensure sound sleep. We have been informed by men working in this area that their work is so hard, uninteresting and monotonous that it would be impossible for them to get through it every day if they did not take this beverage. In fact many become so used to it that they are unable to work if they do not get it and similarly the prospect of getting it is often an incentive for work.

(4) *Social, religious and ethnological factors.*—The use of *pachwai* is considered necessary at religious and social festivals by Sonthals, Garrows, Koch, Dhangars, Mandais, Tipperas and other similar aboriginal tribes. The Sonthals, especially the women, object to the use of *pachwai* that is bought from a shop.

There is a general belief amongst the hill tribes that fermented liquors are less injurious than distilled spirits. The use of these fermented liquors is not only permitted but sometimes it is encouraged by custom. On the occasions of religious worship amongst many of the backward races inhabiting the Western Ghats and in the hilly tracts between Chota Nagpur and Godavari, the use of these liquors is considered necessary. Men, women and children all indulge in these drinks, there being no restriction as to caste or creed. Among the Sonthals and Bhumij tribes of Chota Nagpur these liquors are considered to be indispensable at funerals, marriages and other ceremonial occasions. The Mohammedans are forbidden by their religion to take alcohol and that is the reason why in the western Himalayas, where the population is predominantly Mohammedan, these liquors are not much used.

Ethnological factors.—It has been said that the Aryans and the white races who introduced the use of alcohol from their original home in central Asia have grown more temperate, while the races of aboriginal stock all over the world, who have been less exposed to the use of alcohol, are more prone to get addicted to its use and to abuse it. Our experience among the races using these beers is that if they can get stronger distilled liquors they will always drink to excess, and drunkenness from this cause is common where economic conditions allow primitive peoples to buy stronger drink. Fortunately this is not very often the case and their means do not usually allow them to go beyond the cheap beers.

Mode of consumption.—In their own homes the amount consumed as a rule is not large but in the licensed shops these people are liable to take larger quantities. The usual dose varies between one to six bottles ($\frac{1}{2}$ pint capacity) daily for an adult man and usually four to six bottles are sufficient to produce exhilaration and mild intoxication. We have however seen persons who can take the weaker beverages the whole day long without any apparent signs of intoxication. The habitués usually assemble in the evening in one of the licensed shops where they sit and drink in company. In the mining areas of Bengal and Bihar there are a large number of shops and any afternoon, particularly on Saturdays and Sundays, one can go and watch thousands of these workers indulging in their favourite drink *pachwai*. *Rabra* and *pakhwai* are frequently used in Jaunsar during the working months from April to October. The semi-solid material serves as a food and is also slightly stimulating like other country beers. It is believed to allay the feeling of hunger and it enables men to carry on their work for long periods during the harvesting season. *Pakhwai* and *rabra* are taken all the year round but *mandwa* wine, which is stronger, is taken only on marriage or other festive occasions.

The following data have been collected after a study of a large number of habitués :—

Age of beginning.—In the majority of cases we have examined, the use of these beverages is generally started in childhood. In our series all except a few persons started it before attaining the age of adolescence.

Present age of consumers.—An analysis of the cases collected by us shows that as many as 70 to 75 per cent of the drinkers are between the ages of twenty and forty years. The highest number of habitués falls between thirty and forty years of age, next in order being those between twenty and thirty years. The number of those indulging in beer after fifty is comparatively small.

Dosage.—More than 50 per cent of our series took up to two bottles ($\frac{1}{2}$ pint capacity) a day, 30 per cent two to four bottles daily and the

persons among the sections of the population who use beer in this way must be very small indeed.

The witnesses who appeared before the Indian Excise Committee (1905-06) expressed the opinion that even excessive use of these beers is less harmful than that of strong spirituous drinks so long as the liquor drunk is not contaminated with deleterious substances. Bedford carefully studied the question of the alcoholic contents and by-products contained in these beers. In point of by-products he found that these beers undoubtedly contain a high percentage of acidity and a much higher proportion of fusel oil. The quantities of furfural present however was less than in country spirits. The beer drinkers therefore consumed comparatively small quantities of alcohol but very much larger quantities of the by-products (except furfural). The general consensus of opinion was, and this is borne out by our own recent observations, that fermented liquors are very much less harmful in their effects than the spirits containing a high percentage of ethyl alcohol.

A large amount of experimental work was carried out by Bedford (1905-06) and recently by Chopra (1927) on both animals and men regarding the toxic effects of alcohol itself and the various by-products of fermentation. The conclusions arrived at by these observers are in accord with each other. These are (a) that alcohol alone is at least as deleterious as alcohol plus by-products, (b) that whilst the by-products are undoubtedly noxious in amounts far exceeding those found in potable liquors, in the relatively small quantities found even in the worst samples of the liquors analysed, their action would appear to be unimportant and negligible and (c) that spirit drinking is more noxious than the drinking of fermented liquors because the toxic amount of alcohol absorbed is more quickly reached and more easily exceeded. Alcohol and not the by-products is chiefly responsible for all the toxic effects produced by potable spirits. Any evil effects observed were more attributable to the excessive quantity of alcohol consumed than to any specially deleterious by-products.

From the experimental data obtained and from our observations in different areas, we are in a position to conclude that these fermented liquors do not produce any special harm when the concentration of alcohol is low and the consumption is not excessive. The age-long experience of the hill tribes in India points to the fact that fermented beers are on the whole less harmful than distilled spirits. The by-products are not harmful in the concentrations in which they are present in these liquors unless very large quantities are taken for prolonged periods. During the course of our inquiry we have not found any greater preponderance of cirrhosis of

the liver or any of the other conditions usually attributed to the excessive use of alcohol among these races than are ordinarily met with in races who do not use these liquors.

From our own observations in different parts of the country where these liquors are used we have come to the conclusion that the use of these fermented liquors is less harmful, and that the country spirits and other distilled liquors are more injurious, because with these strong drinks the toxic limit of alcohol to the human system is more quickly reached and is more easily exceeded.

Any attempt at suppression of these liquors will probably lead to more extended use of distilled spirits or harmful drugs among these races. Home-brewing, in the areas in which it is allowed, appears not to be causing drunkenness and deleterious effects generally. A quite different factor responsible for ill-health in the consumers is the insanitary conditions under which these beers are manufactured. The utensils may not be properly cleansed and impure water be used in the preparation, and to these facts might be attributed the occurrence of diseases such as dysentery, diarrhoea, cholera, tuberculosis, typhoid, etc. Finally it must be mentioned that beers after storage may taste stale and sour on account of bacterial contamination when by-products, such as acetic acid and lactic acid, are formed. The harmful effects of these drinks appear to be due more to the unsatisfactory methods of preparation and storage than to the actual harmful effect of alcohol proper.

REFERENCES

- Chopra, R. N. (1927). The Deleteriousness of Potable Spirits on the Indian Market. *Indian Med. Gaz.*, Vol. LXII, p. 195.
- Chopra, R. N. (1927). Observations on the Toxicity of Mature and Immature Genuine Spirits and Imitation or Facitious Spirits. *Indian Journ. Med. Res.*, Vol. XIV, p. 1005.
- Chopra, R. N., and Chopra, G. S. (1932). Chloral Hydrate and Paraldehyde as Drugs of Addiction. *Indian Med. Gaz.*, Vol. LXVII, p. 481.
- Hutchinson, C. M., and Ram Ayyar, C. S. (1915). *Bakhar: The Indian Rice Beer Ferment. Memoirs of the Department of Agriculture in India. Bacteriological Series.* Vol. I, No. 6.
- Ray, J. C. (1906). Hindu Method of Manufacturing Spirit from Rice and its Scientific Explanation. *Journ. of Asiatic Society of Bengal.* Vol. II, p. 129.
- Ray, N. K. (1932). A National Drink of the Hill Folk of Darjeeling. *Indian Med. Gaz.*, Vol. LXVII, p. 551.
- Thomson, J., and others (1907). *Report of the Indian Excise Committee, 1905-06.* Calcutta: Supdt., Govt. Printing, India.
- Watt, G. (1891). *Dictionary of the Economic Products of India.* Vol. V, p. 124. Calcutta: Supdt., Govt. Printing, India.

Drunkenness.—This is largely dependent on the locality. Some of the races drink these liquors to intoxication if opportunities present themselves. The hill tribes of Bengal will take large quantities if they can get the products ready-made in shops, but on account of the paucity of the supply of rice they are not inclined to manufacture beers in their own homes. Drunkenness with *pachwai*, which is considered to be a comparatively mild and wholesome drink, is not an uncommon occurrence in the mining areas in Bengal and Bihar. The evidence in favour of *pachwai* being taken mostly for its nutritive effects is also not so strong as in the case of such beers as *zu* and *laopani*, as the rice in the former becomes unpalatable and bitter after fermentation, and is not consumed but is thrown away.

In Assam among the hill tribes the beers ordinarily consumed are weaker and the manner of their consumption is different, the liquor being taken in the form of a thick gruel and the rice eaten with it. It is a part of the dietary of the inhabitants of the whole range of hills right up to Tibet and Burma. These tribes, who have a fine physique and are hardy, use as much as 25 per cent of their rice crop for this purpose. This in itself is a proof that this beer cannot be very harmful. Drunkenness of a convivial kind however does occur among these tribes and many individuals become incapacitated for days together after these bouts. Among tea-garden coolies things are much worse and there is considerable drunkenness from this cause. The coolies get so habituated to the use of these beers that they will starve themselves in order to get rice for brewing *laopani* or *zu*. On these grounds some of the local officials have urged the total suppression of these liquors. On the other hand, others are of the opinion that any attempt to restrict their production would do more harm than good and would encourage drinking of stronger liquors. From our own observations on these drinks in different places we are inclined to agree with the latter view.

In the United Provinces all the evidence goes to show that excessive use of beers and drunkenness is confined chiefly to festive occasions. In Jaunsar taluk *pakhwai* and *rabra* are mainly used on such occasions as New Year's day, Dewali and certain other festivals. In the Punjab evidence of drunkenness and even of debauchery was produced before the Excise Committee, but as a rule *lugri* drinking is only conducive to merry-making of a harmless type. In southern India these beers are used to a much smaller extent, there being only one or two small areas where they are still consumed. The use of beers to the extent of producing uncontrollable intoxication is rare. Repeated doses of these liquors, particularly when undiluted, may produce a state of intoxication similar to

that commonly produced by stronger forms of alcoholic drink. The accompanying regardlessness of danger and feeling of bravery induced in such cases is partly the result of the temperament of these more-or-less primitive races, but it is also in many cases due to a state of mental confusion induced by poisons such as *dhatūra*, *aconite* and *nux vomica* that have been added to these beers.

In addition to such instances of intoxication where there is a distinct motive, there are some cases that correspond to those of alcoholics in western countries. There are, however, few instances of the type of drinker amongst these country beer-consumers who intoxicates himself with these liquors for the sake of being intoxicated. From our observations we are justified in concluding that gross instances of producing motiveless drunkenness from country beers, corresponding to the excessive drinkers of alcohol in the western countries, are very rare.

Withdrawal symptoms of a mild type rarely occur even among those who habitually indulge in excessive doses of these liquors, they occur more commonly among those who consume distilled liquors in addition. Such persons state that when the drink is not obtained they feel a strong desire for it and that they become very depressed. In some, a feeling of chilliness and disinclination for work accompanied by loss of appetite is observed. In such cases a glass or two of these drinks will restore them to their normal state of health and mind.

Deleterious effects of beers.—During the last two years we have visited most of the areas where these liquors are used and have been able to study a large number of their users. From the data collected it is clear that the habitués may be grouped into two main classes with regard to the effects produced by these drinks.

The first are the tribes inhabiting the Assam hills and hill tracts right down to Burma, who use beer as an article of dietary or as a bland and mildly-stimulating drink. The Nagas drink these beers in lieu of water, and these hill tribes are noted for their fine physique in spite of using beer on a most extensive scale. We have not been able to detect any mental and physical deterioration in habitués of this class. All these persons are useful members of society and carry out their vocations in life which involve very hard physical work.

To the second group belong those who use beer primarily for the intoxicating effects produced by alcohol. To this category belong most of the races living in the plains and low-lying hills.

Both classes undoubtedly contain a certain number of psycho-neurotic individuals who are unable to bear the strain and stress of life and resort to these liquors, but the number of these

involvement of the musculospiral nerve. He can carry heavy office chairs and do the work that might be expected of an ordinary coolie with ease, *see figure 3*, and with his clothes on it is difficult to suspect that the arm has been injured in the manner described.

The individual is above the average in muscular development and gives the impression of being a remarkably tough fellow of unusual vitality.

This is the first case of this nature that I have seen, but recovery of function to a remarkable degree after failure of union would appear



Fig. 3

to be a special feature of injuries in this region, as a remarkably similar case is described by Sir John Coolie in his book, *Fraud in Medico-Legal Practice*, page 11. Sir John Collie describes his case in detail to illustrate the need for thorough examination in medico-legal work. His patient, a sailor, had done strenuous able-bodied work for 18 years and was at great pains to conceal his disability. He boasted, after exposure, that he had deceived between

20 and 30 doctors to whom he had been sent for physical fitness examinations.

The individual whose condition is described in this note had been sent to me for the usual periodical medical examination for physical fitness and visual acuity prescribed for railway employees. He was, like the sailor, very keen to prove that he was fit in every way.

As a railway surgeon I am not infrequently concerned with compensation cases under the Workman's Compensation Act, and it is of some interest to speculate on the possible outcome of this man's injuries had they occurred to-day under the present rules. The assessment of his present disability would certainly present difficulties.

Pseudarthrosis after non-union of fracture does not appear to be as common in the upper arm as in the forearm, where, if both bones are fractured, non-union with a false joint is more likely to occur than in any other part of the body. As a rule the only satisfactory treatment is bone grafting. This man was offered an operation of this type but refused. In his state of life I think he was wise.

I have to thank Dr. R. V. Clayton, M.B., D.P.H., D.M.R.E., Principal Medical and Health Officer, G. I. P. Railway, for permission to publish this case, and my assistant Dr. M. Roskino for the illustrations and radiogram.

VOLVULUS OF THE SIGMOID

By P. BANERJEE, F.R.F.P.S., F.A.C.S., F.R.S.E.

MAJOR, I.M.S.

Civil Surgeon, Bakarganj

VOLVULUS is possible in any portion of the intestinal tract from the stomach to the sigmoid colon. Thus volvulus of the stomach, due to gastropexia, an hour-glass contraction or certain kinds of injury, although extremely rare, is known. Volvulus of Meckel's diverticulum when it is persistent is recorded. Similarly volvulus of the small intestines, the ileo-caecal junction or even of the caecum occurs but very rarely. The commonest volvulus is that of the sigmoid colon. This portion of the colon, on account of its peculiar anatomical structure in having a very narrow-based but long mesentery which spreads out in a fan-shaped manner, is easily susceptible to twisting. The length of the loop suspended from this narrow mesentery varies from nine to about twenty inches and it is extremely mobile. The two ends of the loop are very closely approximated owing to the nature of the mesentery. The narrower the base of attachment which may be a normal condition or may be caused by inflammatory adhesions, as a result of infected lymphatic glands, or chronic inflammatory and ulcerative conditions of the loop itself, the greater is the tendency of the bowel to be twisted. The lengthening of the bowel on

PSEUDARTHROSIS OF HUMERUS

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THE following case appears worthy of record and may be of interest to practitioners who are concerned with cases of injuries 'arising out of and in the course of employment'. It illustrates the extraordinary powers of recuperation and adaptation possible in the human subject.

M. S., employed as a gateman in the railway service, aged 45 years, was injured on duty while working as a porter about 15 years ago. The left humerus sustained an open comminuted fracture about its middle, and the upper end of the left femur in the region of the great trochanter and the neck was comminuted without any external wound. A radiogram of the upper end of the left femur showed an extensive healed fracture. He was treated in the railway hospital and was able to walk after about five

from abnormal stresses in the joints of the left lower limb. The left arm has a gap in the bone about the middle of the shaft, the soft tissues between the ends being about three inches in circumference. The radiogram, figure 1, shows



Fig. 1

months. Several pieces of bone were removed from the wound in the upper arm before healing was complete. He was provided with a job as a gateman and has performed this work satisfactorily ever since. He walks with only a slightly perceptible limp although the left limb is $1\frac{1}{2}$ inches shorter than the right. There is no evidence of a compensatory scoliosis and the radiogram does not reveal any osteoarthritis

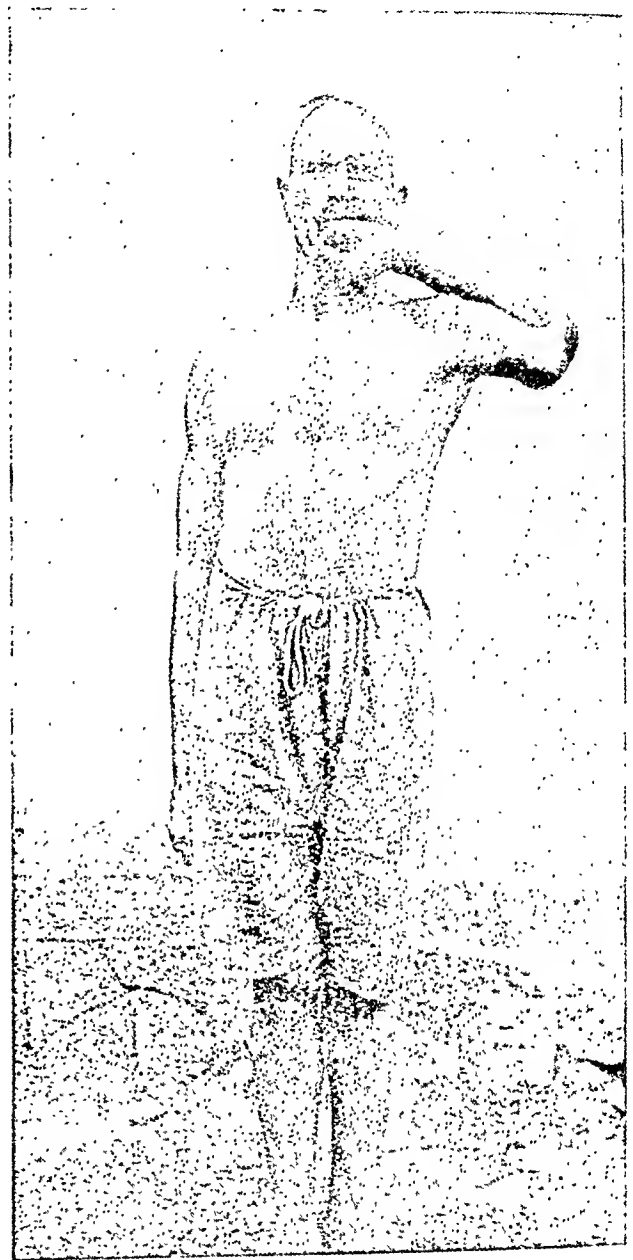


Fig. 2

an irregular rounding of the bone ends with complete closure of the medullary cavity. Four small shadows of isolated fragments of bone can be seen between the broken ends. Great mobility exists at this pseudarthrosis. Figure 2 illustrates the extraordinary range of movement possible in the arm. To attain the posture figured some assistance from the right hand was used to swing the injured arm behind and above the head. The arm of course cannot be extended at full length but considerable muscular power can be exerted when the arm is used with the false joint flexed. The muscles of the arm are well developed and there is no wasting, as can be seen from the illustration. There is no

increased, and thus the normal pulse and respiration ratio is disturbed.

Except in the very early case, when an attempt may be made to relieve the condition by passing a flatus tube once, no delay should be made in opening the abdomen. When operation is performed early, the volvulus is easily recognized directly the abdomen is opened. In late cases, however, along with the twisted portion of the colon other distended coils of large bowel are seen and it is difficult to make out which is the twisted loop. I have, however, found that the twisted loop of sigmoid presents a different colour from that of the others. It will be found to have a greyish-blue colour in contrast to the rest of the dilated large bowel, which has a reddish-purple colour. The difference in colour is certainly due to the practically complete obstruction of circulation in the twisted portion of the bowel. It is not seen in cases where there is only half a twist, as in these the sigmoid with the rest of the large bowel has the same colour. Where gangrene has already set in and the patient's condition is very low, no attempt should be made to resect the bowel, but if possible the twist should be undone and the gangrenous loop brought outside the abdomen and excluded, after dividing it above and below, from the rest of the sound bowel.

The separated gangrenous loop and the openings above and below it should then be fitted with Paul's tubes for lavage and drainage. Immediate resection and anastomosis in a patient suffering from a high degree of toxæmia and shock very often prove fatal in India even when the operation is performed quickly. But it may be done later when the condition of the patient has improved. When gangrene has been extensive, necessitating removal of a very long piece of bowel, even end to end anastomosis may not be possible. The only course then left is to create an artificial anus as in colostomy with the lower end of the descending colon and close the upper end of the rectum.

If only one or two small patches of gangrene are seen these may be excised and the openings closed by purse-string sutures covered by Lembert stitches.

In certain cases, one may find the loop so fixed by adhesions at the point of the twist that it cannot be untwisted. Of course the only immediate surgical measure then possible is to drain the upper and lower limbs of the loop. I have myself not seen such a condition.

In the generality of cases, I suggest the following operation :—

The abdomen should be opened on the left side by a left paramedian incision extending from three to four inches above the umbilicus to an inch or an inch and a half above the pubic symphysis. The abdomen is entered from the inner side of the rectus muscle. In very early cases the volvulus will be found occupying

partly the pelvis and partly the lower abdomen, and the loop will be easily recognized from the rest of the distended colon by its peculiar colour which I have described above. It should be carefully taken out and untwisted. So long as the distended loop is not extracted from the abdominal cavity, it is difficult to determine the direction of the volvulus. I consider it therefore necessary for it to be brought out of the abdominal cavity. As soon as it is untwisted a rectal tube should be passed to relieve the dilatation by letting out any gas and as much of the fluid faeces as possible. More than one tube should be kept at hand as they get rapidly choked with faeces.

In a case where the dilatation is extreme and the loop occupies the whole of the abdominal cavity reaching up to the under surface of the diaphragm, it is inadvisable to attempt to drag it out of the abdomen even through a large opening. In the attempt the bowel may easily be ruptured. In such circumstances, the part of the distended bowel, which presents itself in the abdominal opening, should be punctured to relieve the distension, every care being taken to prevent contamination of the peritoneal cavity. This opening should be closed with purse-string and Lembert sutures as soon as the distension is relieved. It will be easy now to bring out the volvulus and untwist it.

It is a well-known fact that recurrence of volvulus is frequent because the pathological condition which causes it cannot be remedied. Plication of the mesentery to shorten it, fixation of the bowel to the lateral parietal peritoneum, and lateral anastomosis between the two limbs of the sigmoid loop have all failed to prevent recurrence. Resection of the loop and anastomosis have been recommended. This is, however, a very severe operation for a patient in a state of shock and toxæmia. I think that a lateral anastomosis between the two limbs of the loop, followed by fixation of the upper limb to the parietal peritoneum laterally, will be found effective and is certainly less severe than resection and anastomosis. The lateral anastomosis must be large, at least four to five inches in length. Thus the canal will be short-circuited for the passage of faeces, and the loop will practically cease to exist. It will form a single tube fixed to the abdominal wall.

Where the sigmoid loop is very long it may be lifted out of the pelvis, its upper limb laid parallel to the descending colon and fixed to it by lateral anastomosis, the lower limb being fixed to the iliac parietal peritoneum.

The limb to be fixed should be stretched and laid parallel to the parietal peritoneum on the lateral abdominal wall nearest to it and then stitched to it by a continuous catgut suture passed through its anterior longitudinal band.

The operation should be performed under local infiltration anaesthesia preceded by a

(Continued at foot of next page)

account of its being constantly loaded from chronic constipation is yet another factor which predisposes to volvulus. All these factors lead to thickening and fixation of the narrow base of the mesentery and thus the parietal attachment forms an axis round which the bowel may readily get twisted.

The exciting factor may be sudden and excessive peristalsis or an excessive accumulation of flatus or strain in a constipated person due to an effort to evacuate the bowel. Indeed in many cases the exciting factor is so insignificant that it cannot be discovered from the history of the case. Even a sudden change in the attitude of the patient has brought it about.

The extent of the rotation varies from a half turn to two or even three complete turns. It generally takes place from right to left, that is in the direction of the hands of a clock. The position of the bowel after volvulus varies considerably. Where the rotation takes place with the loop more or less in the pendulous position, and if the case is seen early, the volvulus lies mostly in the pelvis in front of or behind the rectum, that is in the lower part of the abdomen and on the left side. If unrelieved, the distension of the bowel increases and the twisted loop, gradually filled up with gas, moves upwards and to the right. With increasing distension of the volvulus the large bowel above the twist also begins to dilate, and in a short time the whole abdomen is enormously distended and respiratory embarrassment is noted.

When the twist takes place with the loop already dilated and lifted out of the pelvis by gas, the volvulus occupies most of the left side of the abdominal cavity with only partial encroachment on the right side and into the pelvis. In either case the coils of small intestine are collapsed by compression.

In certain cases the distension of the bowel is so considerable that the longitudinal muscular bands cannot be recognized.

If the twist is complete and tight so that there is almost total disturbance of circulation which occurs in most cases, the changes in the wall of the loop are rapid, and the wall becomes cedematous and congested. Hæmorrhage from minute vessels in its walls takes place and exuded serum and blood dilute any faecal matter that may be present. With further progress of the constriction, effusion of sero-sanguinous fluid into the general peritoneal cavity may occur. This has been stated by some authorities as diagnostic but in my experience it is rare and I have so far noticed it only in one case. If the volvulus is still unrelieved, patches of ulcer appear in the mucous membrane of the bowel and later small areas of gangrene are noticeable on the serous coat. I have seen both these conditions but I have never seen perforation even in very advanced cases. Perforation when it does occur is usually said to be found above the obstruction.

The gas which fills the distended bowel is certainly the result of putrefactive processes, which follow the condition. A puncture of the bowel leads to the escape of an offensive gas and some fluid fæces.

When the twist is not complete and not very tight, the distension is not so extreme and some fluid fæces mixed with blood and flatus may be passed.

The onset of the disease is always sudden and is ushered in with a fairly sharp pain in the region of the left iliac fossa followed by absolute constipation. In the early stages the pain in the iliac fossa is from time to time augmented by colicky exacerbations. The dilatation is so rapid that soon pain and tenderness are complained of all over the abdomen. This, however, is inconsiderable and of an indefinite character and is, I think, due to the tremendous dilatation putting the serous coat of the bowel and its mesenteric attachments on the stretch. The dilatation causes a drum-like note on percussion. Absolute constipation and the sudden sharp pain, which mark the onset of the disease in a patient who is habitually constipated, are important points in diagnosis. The initial pain in the iliac fossa and its colicky exacerbations last only for a very short time and thus I have been able very rarely to elicit this history from a patient.

Early cessation of colic is no doubt due to early muscular paralysis of the large intestine, and this is proved by the fact that even in a case seen in the early stages, when, on untwisting the volvulus, the flatus tube is passed, the escape of gas is purely mechanical and has to be helped by gentle pressure on the gut. The collapsed bowel after evacuation still retains its abnormally large calibre, and is helpless for days to evacuate whatever may be drained into it from the small intestine. When this is remembered it will be realized how important it is in post-operative treatment to evacuate the bowel by lavage and flatus tube for some time afterwards.

Complete disappearance of pain and tenderness over the abdomen I have found a very bad omen. The pain generally disappears with the onset of gangrene and such cases always prove fatal.

Toxæmia is rather slow in onset as compared with other varieties of acute intestinal obstruction, no doubt owing to very slow absorption as a result of almost complete obstruction of arterial, venous and lymphatic circulation.

The temperature remains normal till very late in the condition when it may become sub-normal. The pulse rate and respiration in the early stages are also practically normal. Indeed I have often noticed the pulse rate and respiration to be slower than normal. But with increase in abdominal distension late in the course of the disease respiration becomes more frequent while the pulse rate is only slowly

PHRYNODERMA : A CONDITION DUE TO VITAMIN DEFICIENCY

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THE symptoms, pathology, course and complications of such deficiency diseases as pellagra, beriberi, and scurvy are well defined, even if the final details of their ætiologies have not been decided. But these are conditions which are familiar to many medical men who work among the indigent classes of the tropics and to which they refer by such indefinite terms as marasmus, malnutrition, deficiency dermatoses, diarrhœa and dysentery due to bad food.

Many years ago in East Africa I was concerned medically with gangs of African labourers working on the construction of the Magadi Railway and the Magadi Soda Factory. These labourers were recruited from their villages, more or less as indentured labour, for a period usually of three months. The healthy only were recruited. They arrived with healthy shining skins. They worked hard for long hours building embankments, etc. The majority of them were fed on maize meal only, it was called *poocho*, and there were few, if any, means by which they could augment this diet.

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descending part of the duodenum. The right testis hangs a quarter of an inch lower than the left.

We have not found any antero-posterior transposition of the viscera. Such a specimen showing general transposition of the viscera with a tricoelian heart described by Adrian Stokes, of Trinity College, Dublin, in the *Journal of Anatomy and Physiology*, 1909, page 301, is of particular interest. A newly born, well-developed male child lived only for a few minutes and died in spite of artificial aid. On post-mortem examination, it was found that in addition to the general transposition of the viscera in the lateral plane, there was also antero-posterior transposition only with regard to the ascending aorta and the stem of the pulmonary artery, so that the ascending aorta was situated in front and to the left of the pulmonary artery. The heart showed only three chambers, two auricles and a common ventricle. The common ventricle was divided by an incomplete septum into two unequal parts, a large right and a small left. Both the aorta and the pulmonary artery opened into the left part of the ventricle, whereas the right part communicated with the pulmonary (right) auricle through the auriculo-ventricular orifice. The pulmonary (right) auricle communicated with the systemic (left) auricle through the foramen ovale and the systemic auricle had no direct communication with the common ventricle.

Within a few weeks their skins lost the natural gloss, and a close inspection showed dry goose skin due to enlargement of the sebaceous glands. They became emaciated, the papules of the skin enlarged, and the epidermis became dry and furfuraceous, a mild form of neuritis was common among them, diarrhœa set in and in many cases was soon followed by death. A similar disease was prevalent among the porters of the Carrier Corps during the war in East Africa. Such a term as marasmus, general debility or dysentery was considered a sufficient description of the cause of death.

I think this picture will be familiar to others who have had experience of gangs of improperly-fed native labourers.

Recently I inspected a jail with a population of over 1,500 prisoners where there was an outbreak of a skin eruption, often accompanied by signs of neuritis, xerophthalmia or keratomalacia, and diarrhœa or dysentery.

There were 87 patients in the prison hospital and the majority of them had papular dry skins. There were 19 in the advanced stages of this, all had diarrhœa or dysentery, and neuritis in a mild or advanced form, and 11 of them showed signs of keratomalacia.

The medical officer stated that the patients did not usually recover from this advanced condition, and that it was customary to consider that death was due to dysentery.

This preliminary inspection indicated the necessity for detailed enquiry into the conditions existing in the prison. The prison authorities kindly supplied the following table of statistics:

TABLE I
Death rate and sick rate in the prison*

	DAILY AVERAGE SICK		DAILY AVERAGE NUMBER OF PRISONERS IN JAIL		DEATHS IN PRISON HOSPITAL	
	Prison hospital	Prison dispensary	Convicted	Unconvicted	Dysentery	Other diseases
1931 ..	75.92	92.4	1,220.4	37	26	28
1932 ..	97.8	120.4	1,463.8	47	40	21

* Needless to state executions are not included in the above statistics (table I).

The sick rate is high and this is reflected in the death rate of 43 per 1,000 for 1931 and 40 per 1,000 for 1932.

The true death rates are higher than these figures indicate, because prisoners who are suffering from incurable diseases and are considered likely to die are sometimes pardoned and discharged to their homes. During 1932 nineteen prisoners were medically boarded for this purpose and recommended for discharge, but, before

COMPLETE TRANSPOSITION OF THE VISCERA

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and

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THE body of a boy, aged two years, who died in the hospital of infantile biliary cirrhosis was dissected in the Mysore University Medical College. This body showed complete trans-



position in the lateral plane of both thoracic and abdominal viscera, the picture presented being an exact mirror image of a normal body.

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hypodermic injection of morphine and atropine. Use of general anaesthetics such as chloroform or ether often brings about pneumonia and a fatal result in a case already toxæmic. The twisted loop of bowel is generally quite insensitive even when its mesentery is stretched or the loop itself squeezed in the course of the operation. Where there is considerable mental uneasiness and the patient demands chloroform or ether anaesthesia an ether mask put over the face often suffices to quieten the nervous patient.

I have performed the operations described above (lateral anastomosis with fixation of the upper or lower limb to the lateral parietal peritoneum) in several cases without recurrence.

Such abnormalities though recorded by various authors are rare, and we are reporting this case as it is the first complete transposition met with by us in the dissecting room.

Cardio-vascular system.—The heart, with the apex pointing to the right, is situated on the right side of the chest with its cavities similarly transposed. The ascending aorta is situated to the left of the pulmonary artery, in the normal slightly posterior plane, the arch of the aorta running from left to right and the descending thoracic aorta running along the right side of the vertebral column. The innominate artery divides into the left common carotid and the left subclavian arteries; the right common carotid and the right subclavian arise independently to the right of the innominate. The right innominate vein obliquely crosses the great vessels superficially from right to left and joins the left to form the superior vena cava which is situated to the left of the median plane. The inferior vena cava is situated on the left of the vertebral column and the two venæ cavæ open into the left atrium.

Respiratory system.—The right lung has only two lobes and presents the cardiac notch along its anterior border. The left lung does not clearly show three lobes, as would be expected.

Digestive system.—The liver (which is much enlarged by disease) is situated on the left side with the larger lobe to the left. The structures in relation to its visceral surface are transposed. The fundus of the stomach is situated on the right side of the cardiac opening which is itself situated to the right of the median plane. The pyloric end is directed to the left and joins the duodenum. The duodenum commences on the left side, has its concavity directed to the right, enclosing the head of the pancreas, the duodeno-jejunal flexure being situated at the level of the second lumbar vertebra to the right of the median plane. The mesentery is attached to the posterior abdominal wall along a line running from the right side of the second lumbar vertebra to the left sacro-iliac articulation. The cæcum is situated in the left iliac fossa with the appendix attached to its right side, about three-fourths of an inch below the ileo-cæcal junction, the free border of the meso-appendix having its concavity directed to the right. The ascending colon and the hepatic flexure are situated on the left side, the splenic flexure and the descending colon being situated on the right, and the sigmoid colon situated on the right side of the pelvic cavity ends in the rectum. The spleen is situated in the right hypochondrium with its hilum facing the left side. The remains of the thymus are present in the superior mediastinum superficial to the great vessels.

Genito-urinary system.—The left kidney is situated half an inch lower than the right kidney and its hilum is in relation anteriorly with the

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Prison dietary

Unconvicted prisoners are placed in the remand jail, and their daily diet is as follows :—

Rice, 22 ounces.
Fresh fish, 2½ ounces, 1½ ounces when cooked.
Or Dried fish equivalent in weight of fresh fish.
Plantain, 2 ounces.
Vegetables, 2 ounces.
Sugar, ½ ounce.
Coconut, ½ ounce.
Lime, ½.
Onions, ½ ounce.
Chillies, 2.
Pepper, 1/10 ounce.
Salt, ½ ounce.

A prisoner after conviction is placed upon a diet known as penal no. 1 for the first 14 days of his imprisonment. Penal no. 2 is served to him for the next 14 days. Thereafter for 11 months he receives ordinary no. 1. After he has served for one year he receives ordinary no. 2 for the remaining period of his sentence.

The following are the diets :—

Penal no. 1

Bread, 4 ozs.
Rice, 18 ozs.
Vegetables, 4 ozs.
Coconut, ½.
Lime, ½.
Pepper, 1/10 oz.
Salt, ½ oz.

Penal no. 2

Bread, 4 ozs.
Rice, 18 ozs.
Plantain, 2 ozs.
Vegetables, 2 ozs.
Dhall, 2 ozs.
* Jaggery, ½ oz.
Coconut, ½.
Lime, ½.
Onions, ½ oz.
Chillies, 2.
Pepper, 1/10 oz.
Salt, ½ oz.

Ordinary no. 1

Bread, 4 ozs.
Rice, 18 ozs.
Fish, 2½ ozs.
Plantain, 2 ozs.
Vegetables, 2 ozs.
Dhall, 2 ozs.
* Jaggery, ½.
Coconut, ½.
Lime, ½.
Onions, ½ oz.
Chillies, 2.
Pepper, 1/10 oz.
Salt, ½ oz.

Ordinary no. 2

Bread, 4 ozs.
Rice, 18 ozs.
Beef or liver, 2 ozs.
Fish, 2 ozs.
Plantain, 2 ozs.
Vegetables, 2 ozs.
Dhall, 2 ozs.
* Jaggery, ½ oz.
Coconut, ½.
Lime, ½.
Onions, ½ oz.
Chillies, 2.
Pepper, 1/10 oz.
Salt, ½ oz.

* Palm sugar.

The following table gives the constituents of the three meals a day for the four diets :—

Meal	Penal no. 1	Penal no. 2	Ordinary no. 1	Ordinary no. 2
Early morning ..	Bread and cunjee, 4 ozs. (Rice gruel).	Bread and cunjee, 4 ozs. Jaggery.	Bread and cunjee, 4 ozs. Jaggery.	Bread and cunjee, 6 ozs. Jaggery.
Mid-day ..	Rice and vegetables.	Rice and vegetables.	Rice and vegetables.	Rice and vegetables.
Evening ..	Pepper water which is made by boiling pepper, salt and tamarind in water.	Rice and vegetables, 8 ozs.	Rice and vegetables, 8 ozs. Fish, 2 ozs.	Beef, 1½ ozs. Rice and vegetables, 6 ozs. Fish, 2 ozs.

The monotony of these diets is somewhat varied in practice, as follows :—

Ordinary no. 1

Mondays—2 ounces of red onions, no fish.
Tuesdays—2½ ounces of fresh fish.
Wednesdays—2 ounces potatoes.
Thursdays—dried fish.
Fridays—2½ ounces of fresh fish.
Saturdays—dried fish.
Sundays—2 ounces potatoes, no fish.

Ordinary no. 2

This is the same as the above, but 1½ ounces of cooked meat is given every day except Friday.

The vegetables consist principally of the following :—One of three varieties of pumpkin is supplied twice a week, and a variety of the following is supplied, according to which are in season, on the other five days :—cucumber, brinjals, snake gourds, jack fruit, bread fruit, bandakka, or drum sticks. Cabbages, tomatoes, spinach and beans have been supplied very occasionally, about once in three months, according to the cooks' statements.

The quantity and quality of the vegetables is such that the diet cannot contain much fat-soluble vitamin. It is probable that there is also a deficiency in B₂.

The penal diets nos. 1 and 2 are particularly deficient. One green plantain weighs between 3½ to 6 ounces and when skinned weighs 2 to 4 ounces. Therefore the amount of vegetables served to each prisoner daily is about the equivalent of one plantain or less.

Most of the prisoners come from the indigent classes, among whom papular dry skin and keratomalacia is not uncommon; therefore it is not surprising, when after conviction they are placed on these diets, that they soon show signs of vitamin deficiency, for the reserves of vitamins in their bodies cannot be high.

Ordinary diet no. 1 differs from the penal diets principally by the addition of a small amount of fish. White fish is usually supplied and this contains very little vitamin A or D (McCarrison, 1921).

The prisoners who have been in prison more than 18 months are less affected than those who have been imprisoned for a shorter period. Probably the addition of the beef which is supplied in ordinary diet no. 2 accounts for this. And this diet may be sufficient to maintain a

effect could be given to this, six died; the remaining 13 were discharged. Furthermore, the aged and infirm are not retained at this prison, but are sent to a small prison at Negombo.

The death rate in Ceylon for the ten years 1921—1930 was 26.2 per 1,000. But the death rate for the Western Province, in which the prison is situated and where malaria is not prevalent, has always been less than this, and in 1932 it was 16.8 per 1,000.

The death rate of a general population is largely determined by infant mortality and the deaths of the aged; both these factors are absent from this prison, and therefore the death rate should not be more than half that of the surrounding population. Thus the death rate in the prison is at least 5 times as high as it should be.

The enquiry was especially directed to skin diseases, neuritis, eye diseases, diarrhoea and dysentery. The medical officer supplied the following table showing the number of prisoners who were treated for these symptoms in 1931 and 1932 :—

TABLE II

		1931	1932
<i>Dysentery.</i> Prison hospital.	Amoebic	38	41
	Bacillary	248	476
	Others	288	246
<i>Dysentery and diarrhoea.</i> Welikada jail. ..		8,359	15,874
<i>Eye diseases.</i> Prison hospital. .. (Keratitis and corneal ulcer.) Welikada jail. .. (Eye diseases.)	..	79	99
	..	1,837	5,866
	..	1,928	7,261
<i>Skin diseases.</i> Prison hospital. .. Welikada jail. ..		237 1,928	151 7,261
<i>Neuritis.</i> Prison hospital. .. Welikada jail.	5	41
	..	1,872	2,397

Although these statistics show the surprising incidence of these conditions, they are even more prevalent than these figures indicate because the diagnosis is given on the predominant symptoms only. For instance the patients in hospital with advanced dry skin, neuritis, keratomalacia and dysentery are considered to be suffering from dysentery and the other symptoms do not appear in the returns. Twenty-one patients being treated for marked keratomalacia were examined, and every one showed signs of papular dry skin.

Examination of working prisoners for papular dry skin and keratomalacia

The method of examination was to line up the prisoners and examine each one and call out the result which was written down by the apothecary of the prison hospital. The prisoner then passed to the apothecary who noted down the date when he entered prison; in this way all bias from a knowledge of the length of time each person had been in prison was avoided. Some of those of the first gangs which were examined complained of burning sensations in the hands and of numbness, tingling and weakness in the legs; others complained of dimness of sight and other symptoms referable to the eyes. But an enquiry into the subjective symptoms of prisoners is an arduous procedure pregnant with error, therefore it was avoided.

The various gangs of prisoners examined were, (a) in the remand jail where they sometimes remain for several months; (b) working in the coir fibre sheds; (c) working in the carpentry shops; (d) working in the laundry.

In the following table (table III) the patients are placed in one of four categories :—

Category I includes those who have been in the prison for less than one month.

Category II includes those who have been in the prison for more than one month and less than one year.

Category III includes those who have been in the prison for one year to 1½ years.

Category IV includes those who have been in the prison for more than 1½ years.

TABLE III

			Total examined	Papular dry skin	Papular dry skin and kerato- malacia	Kerato- malacia only	Skin and eyes more or less healthy	Percentage show- ing papular dry skin and/or keratomalacia
Category I	138	10	Nil	Nil	128	7.2
" II	189	100	11	Nil	78	58.7
" III	38	22	2	2	12	68.4
" IV	111	32	11	2	66	34.6

Photographs taken from prisoners who were working



Fig. 1
Earliest stage

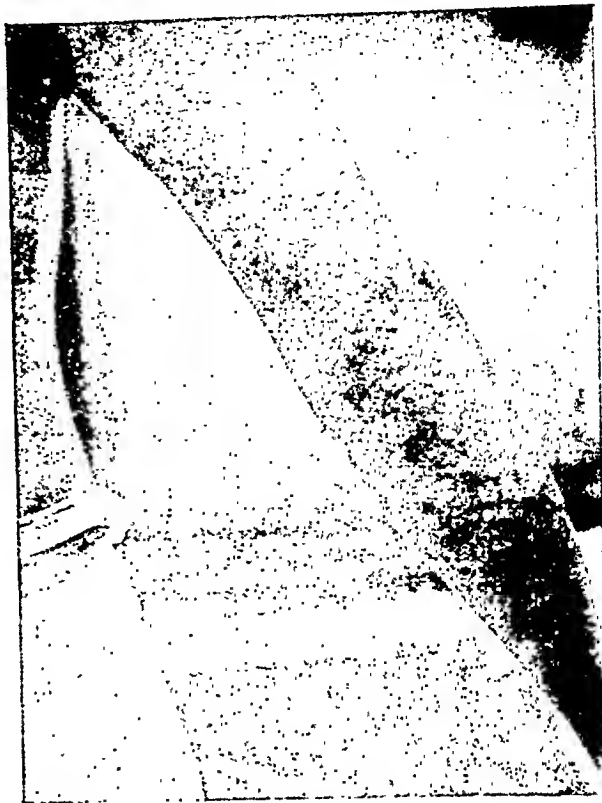


Fig. 2
Early stage

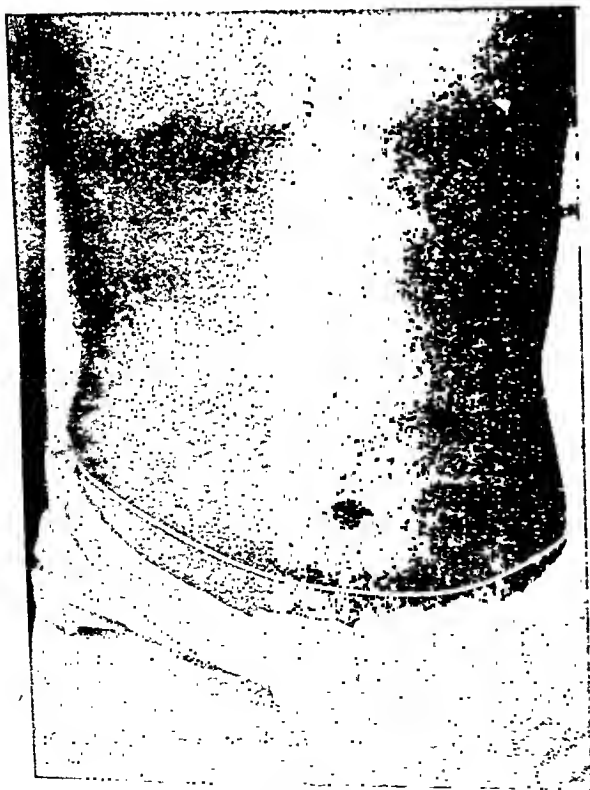


Fig. 3
Later stage



Fig. 4
Later stage. (Inner aspect of thigh)

person in a fair state of health provided he is not given very hard work.

Overcrowding.—The cells and corridors were built to accommodate fewer prisoners than are in the jail at present. There is some overcrowding of the floor space at night, but this is mitigated by the great height of most of the corridors.

THE SYMPTOMS

Papular dry skin.—This commences with the appearance of minute, hard papules, and the surface of the skin becomes dry and loses its natural gloss. The eruption may be irritable and the patients rub and scratch the skin. The papules may occur on any part of the body, but they are particularly liable to occur on the thighs, the extensor surfaces of the arms near the elbows, the abdomen and across the shoulders. They are less common on the face, neck and anterior surface of the chest.

The papules enlarge and many of them become very dark in colour. When examined with a lens the apex of a papule is seen to have a small crater-like opening often with minutely fissured sides. When a papule is squeezed with forceps a dense somewhat-translucent sebaceous material exudes; in some cases this material cannot be squeezed out without incising the papule.

In the later stages the natural fissures of the skin increase in depth and width, and still later the whole skin of the body becomes very dry and furfuraceous, and the papules stand out with dark pigmented areas around them.

The papules do not tend to suppurate, but a dry form of skin sepsis may take place, when hard dry thin scabs form over and around the papules. Removal of a scab leaves a very superficial excoriation of the skin.

The papules are enlarged sebaceous glands plugged with altered sebum. The papules in some cases appear to spread laterally, producing sub-angular, slightly-raised flattened areas of smooth epidermis, contrasting with the surrounding accentuated fissures of the skin; the centres of the areas show the openings of the gland ducts, possibly this is a process of recovery.

In some cases the furfuraceous dry skin is more marked than the eruption of papules, but the latter can always be seen by a close inspection.

The diagnosis of the papular dry skin must be made from scabies and acne.

It is liable to be mistaken for scabies in those patients where there is itching. The distribution of the two conditions is different, scabies occurs between the fingers, on the front of the elbows, around the nipples and on the buttocks; it is seldom so widely spread as the condition of papular dry skin. Scabies is at first vesicular, and later becomes pustular, and the eruptions

due to the sepsis and scratching are not as dry as in papular dry skin.

In acne the itching is more or less absent, and the material squeezed from an acne papule is white, opaque, and caseous in contrast to the somewhat translucent material of papular dry skin. Well-developed acne sooner or later becomes papular, and the sepsis often spreads around the base of the affected gland and forms a small abscess. But this I have not seen in papular dry skin.

Some of the prisoners had pyosis, that is a septic condition of the hair follicles, its commonest site is on the extensor surface of the legs below the knee. It cannot be mistaken for papular dry skin.

The photographs reproduced here are from two early cases and one later case. Many of the papules were darker than these photographs indicate.

Keratomalacia, due to vitamin-A deficiency, is well known in Ceylon. It has been described from India, Africa, and other countries, and I read in the limited references available that it usually starts as a xerophthalmia.

The course of the disease in the prison appears to be as follows:—It starts by injection of the vessels running from the inner and outer canthi of the eye to the cornea; and the redness of the vessels stands out in marked contrast to the whiteness of the sclerotics; at the same time yellowish thickenings occur where the vessels disappear at the corneal-sclerotic junction.

The next change is the appearance of pin-point opacities in the cornea; these increase in size and may become two or three millimetres in diameter. Then the opaque areas ulcerate, and if the ulcers do not heal they become extensive and hypopyon develops, and finally the anterior chamber and cornea become disorganized and permanent blindness follows.

Before the opacities of the cornea have appeared many of the prisoners complain of dimness of vision and even of blindness. The visual symptoms must be due to the deficiency affecting other parts of the eye than the cornea.

Neuritis.—Table II shows that the diagnosis of neuritis was made in the cases of 41 patients admitted to the prison hospital (apart from those with dysentery and neuritis) and 2,397 patients attending the prison dispensary in 1932.

All the patients in the hospital who had advanced papular dry skin, wasting, diarrhoea and dysentery showed signs of neuritis, and in several cases it was so advanced that the patients were unable to stand. But many of the dispensary patients have subjective symptoms only, namely a burning sensation of the hands, and weakness, numbness and tingling of the legs. The more advanced cases showed absence of knee jerks.

A NOTE ON THE VALUE OF THE ASCITIC FLUID FOR THE WASSERMANN REACTION AND AGGLUTINATION TESTS WITH DYSENTERY ORGANISMS*

By M. V. RADHAKRISHNA RAO, M.D., B.S.

Research Fellow, Andhra University

(From the Department of Pathology and Bacteriology, Medical College, Vizagapatam)

THE material in this paper was collected during an investigation into the causation of ascites (Radhakrishna Rao, 1932) and subsequently during a study on decompensated portal cirrhosis, in the medical wards of the King George Hospital, Vizagapatam.

In all the patients who were admitted with ascites into the medical wards of the King George Hospital, Vizagapatam, the Wassermann reactions and the agglutination tests (with dysentery organisms), of the blood and ascitic fluid, were done as a routine, in addition to the other investigations. This short note is based on a study to find out how far the results obtained with ascitic fluid are valuable in these tests, as compared with those obtained from the blood serum.

The results are summarized in tables I and II. In most of the cases specimens of the blood and the ascitic (aseptically drawn) were taken for examination at the same time; while in the others, there was only a short interval between

(Continued from previous page)

The disease occurs in young children, and although neuritis is not mentioned it is probably the same condition as occurs in the prison.

It appears to me that some name is required for this disease. The name *mandama* (pronounced mārndārmār) is almost synonymous with marasmus and therefore is unsuitable.

Dr. Fonseka's mention of a 'frog-like skin eruption' at first puzzled me, because a frog's skin is soft and smooth. Apparently it is a native description of the eruption, and in translating it into English, he has used the word frog, when it should be toad. The skin of a toad is dry, and 'papular', and the feel and appearance of it are very similar to the later stages of papular dry skin.

The disease may have been definitely named previously, but, if it has not, I propose to call it phrynoderma (φρυνη a toad), and to define it as:—'A papular dry skin eruption frequently accompanied by a mild neuritis and (or) eye symptoms such as night blindness, dimness of sight, xerophthalmia, or keratomalacia; the patients are very liable to diarrhoea or dysentery, when this occurs the neuritis becomes more marked; a high mortality results. The disease is due to vitamin-A deficiency, but other food factors may be at fault'.

* Rearranged by Editor.

the examination of the blood and the ascitic fluid.

It will be seen that out of the 60 cases, in which the Wassermann reactions of the blood and the ascitic fluid are compared, the results of the latter tally exactly with those of the former in 37 cases. However, if the ++ and + results and the (±) and —ive results, respectively, are grouped, it will be seen that there is agreement in 51 out of 60 cases.

TABLE I

Showing the comparative results of the Wassermann reaction of the blood and ascitic fluid. [++ = strong positive; + = positive; (±) = doubtful; — = negative]

BLOOD WASSERMANN RESULTS IN GROUPS		ASCITIC FLUID RESULTS OF EACH GROUP	
Result	Number of cases in group	Result	Numbers in group
++	31	++	19
		+	7
		(±)	1
		—	4
+	12	++	5
		+	6
		(±)	1
		—	0
(±)	3	++	1
		(±)	1
		—	1
—ive	14	++	1
		+	1
		(±)	1
		—ive	11
TOTAL	60	..	60

Table II, given below, shows that out of the 53 cases in which the results of the agglutination tests (with dysentery organisms) of the blood and ascitic fluid are compared, 22 cases showed the same reaction in both. Out of these 22 cases, 16 showed negative reaction both to *B. dysenteriae* (Shiga) and *B. dysenteriae* (Flexner).

Out of the 31 cases in which the agglutination reactions of the ascitic fluid did not agree with those of the blood, 5 gave a higher reaction than the blood serum, while in the remaining 26 cases the reaction was in a very low titre compared to that of the blood serum, or negative altogether.

It will thus be seen that, while the results of the Wassermann reactions of the ascitic fluid compare favourably with those of the blood

Bacillary dysentery is a prevalent infection in the prison, and the possibility of the neuritis being due to dysentery was considered. This possibility cannot be excluded in some of the advanced cases in the hospital, although it is very improbable that such a complication of dysentery would occur in all these cases.

But the milder forms of neuritis so common in the prison cannot be due to dysentery, because very few of the patients had had dysentery.

The neuritis closely resembles that of pellagra in its insidious onset.

Diarrhœa and dysentery.—Although there can be little doubt that the papular dry skin, the keratomalacia, and the neuritis are due to vitamin deficiency, the diarrhœas and dysenteries cannot be definitely assigned to this cause. Flexner's bacillus has been isolated from the stools of many patients and the overcrowding of the prison may account for the prevalence of bacillary dysentery.

It is generally accepted that persons who live on a diet deficient in the fat-soluble vitamins are particularly liable to bacterial infections, and these infections are generally very acute.

Monkeys and rats fed on vitamin-deficient diets develop persistent diarrhœa, which as death approaches becomes dysentery.

One of the three cardinal signs of pellagra is diarrhœa.

The course of the disease.—The disease commences as a papular dry skin, and usually there are subjective symptoms of mild neuritis, the patient loses weight, but does not become markedly emaciated. Diarrhœa or dysentery starts, and usually becomes very acute, pyrexia is low, and the temperature seldom rises above 101°F. The skin eruption becomes accentuated, and the neuritis increases, and in two-thirds of the patient's eye symptoms occur. Some of the patients die a few days after the onset of the acute dysentery, but with most of the patients the dysentery becomes chronic, and periods, when the stools become normal, alternate with recurrences of the diarrhœa. In the last stages the patient becomes very emaciated, and is unable to use his legs or arms, the skin becomes very dry and furfuraceous, xerophthalmia or keratomalacia is present, and in a few cases symptoms of dementia occur.

Prognosis is difficult because, although most die, some recover, and others when apparently well on the way to recovery die suddenly.

Post-mortem examinations.—Two post-mortem examinations have been obtained.

A man about 50 years of age was admitted to the hospital with acute bacillary dysentery (Flexner). He was not emaciated, but had papular dry skin and a few opacities in the eyes from keratomalacia. The attack was fulminating and he died in five days.

The post-mortem examination showed the heart, lungs and kidneys to be normal, the spleen weighed 3½ ounces and the liver 40 ounces, the latter showing fatty degeneration. The large intestine showed advanced diffuse coagulative necrosis throughout its length, and the last two feet of the ileum was affected. Obviously this man died of acute bacillary dysentery. But a man of this age would not pass through life in a country where bacillary dysentery is common without acquiring some immunity to the disease, and it is probable that the food deficiency of which he showed symptoms was the primary cause of his loss of immunity.

The second post-mortem examination was carried out on the body of a man who had been in hospital for six weeks. He had had dysentery, and his later symptoms were diarrhœa, advanced papular dry skin, neuritis—he had been unable to stand or feed himself, and had xerophthalmia, emaciation, and signs of dementia. The diarrhœa had ceased several days before death.

The post-mortem findings were:—lungs normal; the heart was carefully examined for fatty degeneration but this was not apparent. The liver showed fatty degeneration and weighed 35 ounces; the spleen weighed 3 ounces; the kidneys showed signs of early 'granular contraction'. There were areas in the large intestine where dysenteric ulcers had healed, but the rectum contained formed faeces free of mucus. The walls of the small intestines were thin and the mucous membrane showed slight superficial erosions, somewhat resembling the condition seen in pellagra.

Had the history of the patient been unknown, it would have been impossible to have stated from the post-mortem findings the cause of death.

Discussion.—Keratomalacia has been described frequently as a symptom of vitamin-A deficiency. But in the literature to which I have access I cannot find references to papular dry skin, associated with neuritis and diarrhœa or dysentery, attributed to vitamin deficiency.

Dr. D. C. de Fonseka, Medical Officer of Health, recently sent to me a short note on a paper which he read before the Ceylon Society of Medical Officers of Health.

He was discussing the Registrars' returns of deaths from rickets. He states that 'it is not true rickets', but is a condition which the local inhabitants call *mandama*. He writes:—'The name *mandama* is given to a condition characterized by eye changes "keratomalacia and xerophthalmia", night blindness, general stunting of growth, frog-like skin eruption, frequent motions with sometimes prolapse of the rectum. There are no bone changes present. The eye condition if untreated leads to blindness'.

(Continued at foot of opposite page)

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It will thus be seen that, while the Wassermann reactions of the blood compare favourably with those

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TABLE II

Showing the comparative results, of the agglutination tests with dysentery organisms, of the blood and ascitic fluid

Agglutination tests (titre)	Blood		ASCITIC FLUID		Number of cases in which the results of the ascitic fluid tallied with those of the blood
	<i>B. dysenteriae</i> (Shiga)	<i>B. dysenteriae</i> (Flexner)	<i>B. dysenteriae</i> (Shiga)	<i>B. dysenteriae</i> (Flexner)	
1/16 ..	1	2	2	1	1
1/32 ..	4	1	3	9	..
1/40 ..	1	1	..	2	..
1/64 ..	1	1	..	1	..
1/80 ..	6	2	1	1	..
1/128	20	..	6	4
1/160	1
1/320	1	..	1	1
1/640	1	..	1	..
1/1280	2	..	1	..
Negative ..	40	21	47	30	16
TOTALS ..	53	53	53	53	22

serum, the results of the agglutination tests (with dysentery organisms) do not, a lower titre than that of the blood serum or a negative result being obtained in most of the cases.

Summary and conclusions

The results of the Wassermann reactions and the agglutination tests (with dysentery organisms), of the blood and the ascitic fluid, collected in a series of unselected cases of ascites, in the medical wards of the King George Hospital, Vizagapatam, are compared in this paper. It is pointed out that, while the results of the Wassermann reactions of the ascitic fluid compare favourably with those of the blood serum, the results of the agglutination tests (with dysentery organisms) do not, a lower titre than that of the blood serum, or a negative result, being obtained in most of the cases.

I wish to express my thanks to Rao Bahadur Dr. T. S. Tirumurti, Professor of Pathology, under whose direction this material was collected and to Dr. C. Ramamurti, Professor of Bacteriology, for permission to publish these results.

My thanks are also due to Dr. N. G. Pandalai and the members of the staff of the Medical Unit of the King George Hospital, Vizagapatam, for their kind co-operation during the collection of this material.

REFERENCE

Radhakrishna Rao, M. V. (1932). *Indian Journ. Med. Res.*, Vol. XX, p. 459.

A CAUSE OF DAMAGE TO OPTICAL GLASS IN THE TROPICS

By H. W. ACTON, C.I.E.

LIEUTENANT-COLONEL, I.M.S.

Director, School of Tropical Medicine and Hygiene, Calcutta

DETERIORATION of the glass of microscope objectives, telescope lenses, prisms and expensive optical glass of all kinds has always been a source of worry to those using optical apparatus in the tropics. Many theories have been advanced to explain this damage, but as far as is known few, if any, of these have ever been definitely proved. In the present investigation, one cause of the clouding of prisms has been definitely established, and a remedy has been suggested. The work is not complete and further research on the lines indicated below will probably produce fresh facts, but it is felt that the matter is of such importance that these notes should be published even in their present state of incompleteness.

Certain prisms were submitted to the writer with a request for an explanation for the clouding of their polished surfaces, which recurred after the glass had been thoroughly cleaned.

The first two prisms submitted showed a fine growth of mycelium on the polished surface; this arose from the region of the unpolished ridge on which there was some wax-like material. Around the hyphæ there was a 'frosted' area which appeared to be formed of deliquescent salts, probably secreted by the hyphæ themselves. In this way the moisture necessary for the existence of the mycelium was produced. Cultures from the hyphæ were made on Sabouraud's and Norris' synthetic media and pure cultures of a *Penicillium* were obtained. Hanging-drop preparations of the hyphæ showed that some of them carried fine conidia or spores arranged in small chains of four or five each which projected as four finger-like processes from the end of the hyphæ. The same growths were seen on the prisms but in these the end-organs of fructification were not so well marked. Four more prisms were received for examination and on these the end-organs could not be seen with a two-thirds objective, but with the corneal lens large spore-like bodies—probably zygo-spores—were seen near the foot of the growth on two of the prisms. The zygospores from these two prisms were inoculated on two tubes and these showed a pure culture of a greenish *Penicillium*.

Inoculation experiments.—Two prisms were sterilized with alcohol and a little lard was smeared on the ridge between the polished surfaces. Spores were inoculated on the ridge and a growth appeared five days later, and after a further eighteen days *Penicillium* was recovered from the prisms. Four other prisms were sterilized and their ridges greased by wiping them with sterile gauze containing grease, they were then inoculated and growth appeared four days later to be followed in a further fourteen days by the appearance of a *Penicillium*. These experiments indicate that the mycelium probably obtains its nourishment from the grease or fat in the mounting material in which the ridge is imbedded, and that it spreads slowly from this point over the polished surface of the prism, the necessary moisture being obtained from the humid atmosphere by the deliquescent salts excreted by the hyphæ.

Tests of different mounting materials.—Lard, grease and beeswax were melted and two agar tubes were smeared with each material, and growth only occurred in the two tubes on which lard was smeared, the other four being negative. Sealing-wax could not be tested in the same way. This experiment indicates that certain fatty substances in lard supply the source of carbon for the fungus, the nitrogen, oxygen and water probably coming from the atmosphere and examination of the prisms with the corneal lens, when first received, suggests that the fungus obtains its nourishment from some fatty matter in the mounting substance. The mycelial growth largely consists of surface runners and

very few conidia, and the formation of zygo-spores shows that the nutriment available for these fungi is very poor.

Tests of the fungicidal properties of various products.—Gentian violet in dilutions of 1/100,000, 1/50,000, and 1/10,000 were first tried, but none had any apparent effect on the growth of the fungus; a dilution of 1/5,000, however, inhibited it for a time but did not entirely prevent the growth.

Copper sulphate in the same dilutions as those used for gentian violet had no inhibitory effect.

Further experiments with 1/1,000 dilutions of gentian violet and copper sulphate were done, and the former inhibited growth for six days whilst the latter had no effect on it.

The essential oils, sandalwood, cinnamon, clove, turpentine and thymol, were tested by making solutions of 1/1,000 strength with 0.1 per cent alcohol as the solvent. A loopful of a three-day-old culture was placed in all of these liquids for the following different periods, half a minute, five minutes, fifteen minutes, half an hour, and forty-eight hours, and the only oil that showed any marked inhibition of growth under these conditions was thymol. Exposure of the fungus to thymol for five minutes caused inhibition of growth for twenty-four hours, and half-an-hour's exposure prevented growth even after forty-eight hours. Cinnamon oil had a similar but slighter effect when the fungus was left in it for one hour. These oils were tested in another way also. Tubes of Sabouraud's medium were prepared which contained dilutions of the various oils in strengths of 1/5,000 and in this case there was complete inhibition with cinnamon oil and partial inhibition with thymol.

Conclusions.—The fungus found growing on the prisms examined is a *Penicillium*.

This fungus can grow on the polished surface of the glass if there are grease spots on it, but it grows more commonly from the unpolished ridge between the prisms where the mounting material is present.

The fungus obtains its supply of carbon from the fatty compounds in the mounting material, and the nitrogen and oxygen are obtained from the atmosphere.

The hyphæ themselves excrete deliquescent salts which during the high humidity in the monsoon enable the fungus to obtain for its growth the very necessary amount of moisture from the atmosphere.

A few substances were tested for their fungicidal properties on this fungus, and of these cinnamon oil was the best, and thymol the next best; the remainder were inert.

THE ANÆMIA OF THE LEISHMANIA-INFECTED HAMSTER

By L. EVERARD NAPIER, M.R.C.S., L.R.C.P.

and

L. R. SHARMA, M.B., B.S., M.R.C.P.E., D.P.H.,
D.T.M. & H. (Cantab.)

(From the Kala-Azar Enquiry, Indian Research Fund Association, School of Tropical Medicine, Calcutta)

DURING our study of the anæmia of kala-azar, a parallel study—on a much smaller scale—of the red cells and hæmoglobin value of the blood of Chinese hamsters (*Cricetulus griseus*) was carried out at the same time. The reticulated red cells of this hamster are shown in the plate (plate X, facing page 550) accompanying this paper (Napier and Sharma, 1933). These results were not included as we hoped to add further observations, but opportunity has not arisen.

The technique was exactly the same as that used in our study of human blood. All the hamsters had been in captivity for at least a year during which time they had been fed on soaked gram and green-stuff (cabbage or lettuce); the leishmania-infected hamsters had been infected for at least six months and in each case the infection was a heavy one, demonstrable by liver puncture. The total red cell count, the reticulocyte percentage and the hæmoglobin value (on the Tallqvist scale) were estimated in ten normal and in ten infected hamsters; the results are summarized below:—

	Normal hamster	Infected hamster
Total red cells—		
Maximum ..	12,000,000	10,312,000
Minimum ..	9,775,000	6,083,000
Mean ..	10,837,000	7,418,000
Reticulocyte percentage—		
Maximum ..	2.60	9.80
Minimum ..	1.50	4.00
Mean ..	2.08	6.38
Hæmoglobin—		
Maximum ..	78	70
Minimum ..	68	55
Mean ..	72.6	62.0

The anæmia in the hamster is thus similar to, though not so marked as, that in generalized leishmaniasis in man; the mean reduction in the red cell count is only just over thirty per cent, against nearly fifty per cent in man; there is a threefold increase in reticulocytes, against a fivefold increase in man; and the decrease in hæmoglobin is apparently only slight (but little reliance can be placed on these readings). If the colour index of the normal hamster is taken

as unity, then the colour index of the infected hamster is apparently well above unity; this is contrary to the finding in kala-azar in man.

The blood changes, as in man, are very constant and in only two instances was the count more than a million away from the mean.

On the whole it may be said that these few observations support the conclusions arrived at in the above-mentioned study of the anæmia of kala-azar in man.

REFERENCE

Napier, L. E., and Sharma, L. R. (1933). The Anæmia of Kala-azar. *Indian Med. Gaz.*, Vol. LXVI, p. 545.

A Mirror of Hospital Practice

A CASE OF CEREBELLAR TUMOUR

By K. G. GHARPUREY

LIEUTENANT-COLONEL, I.M.S.

Civil Surgeon, Belgaum

Y. S., Hindu male, well built, aged 25, Berad by caste, a farmer, was admitted into the Civil Hospital, Belgaum, on 24th July, 1933, for severe headache. He was sent by the patil (headman) of his village, as he used to roll on the ground because of pain in the head. He had received local treatment in the village for three months without any relief.

On admission.—His speech is slow and he walks slowly with a staggering gait. He states that he is losing strength in his right upper and lower limbs. He feels giddy and reels on standing. He states that his vision is failing and that he feels very heavy in the head and has a severe bursting headache. The pain is so intense that he shouts at times. He does not sleep well and has pain and deafness in both ears though there are no signs of external or middle ear disease. There is a coarse nystagmus. Examination of the eyes revealed optic neuritis in both eyes, tending towards optic atrophy in the left eye.

Iodides and bromides with other sedatives gave him no relief. Lumbar puncture was done and 15 c.cm. of clear cerebro-spinal fluid was removed under pressure.

On 17th August, 1933, the patient had an attack of convulsions, resembling epilepsy and died suddenly. At post-mortem examination a white neuroglial tumour of the size of a lemon was found inside the right lobe of the cerebellum. There were no adhesions. A piece of the tumour was sent to the Haffkine Institute, Parel, Bombay, and the report was glioma of the cerebellum. The specimen is preserved to be sent to the B. J. Medical School, Poona.

Headache, vertigo, staggering gait, nystagmus, with optic neuritis—the typical symptoms of a cerebellar tumour—were present.

REMOVAL OF A FOREIGN BODY FROM THE OESOPHAGUS*

By FRANCISCO DIAS

Casa Cirurgica, Dramapur, S. Goa

A CHILD aged four years was brought to me and the following history was given :

She had swallowed one pice some hours before and since that time all food and liquids were immediately vomited. This statement was tested by giving the child some gruel which she was unable to swallow. There was no evidence of interference with respiration.

The coin could be felt in the oesophagus posterior to the trachea about one finger-breadth above the jugular notch. Under chloroform anaesthesia several unsuccessful attempts were made to extract the coin with a pair of long forceps, and it was then decided to try manipulation. The coin was worked upwards by the fingers of the right hand applied externally and when it reached the back of the throat it was easily seized by the fingers of the left hand and removed. Relief was instantaneous and the child experienced no further trouble.

PASSAGE OF A SAFETY-PIN THROUGH THE ALIMENTARY CANAL

By KOKA VENKATA RAMA RAO, L.M. & S. (Mad.),
L.C.P. & S. (Bom.)

Sankar Dispensary, Tenali

A CHILD aged one year swallowed a small brass safety-pin on 8th October, 1933, at 11 a.m.

I gave castor oil one ounce and by 3 P.M. he had three loose motions, but the pin was not passed. At 5 P.M. I administered half an ounce of isaphagul seeds well soaked in water. The next morning he passed a stool mainly composed of round masses the size of a small lime with some faecal matter, and the opened pin was found imbedded in one of these masses.

These seeds are called, English:—Isaphagul or spogel seeds. Telugu:—Isapugolu villulu. Bengali:—Osabgul. Hindi:—Osufgul.

When the seeds are soaked in water they become coated with abundant adherent mucilage or gelatinous substance. I have used these seeds for a long time in chronic constipation.

AN INTERESTING CASE OF COMPOUND DEPRESSED FRACTURE OF THE SKULL

By JAMIAT SINGH, M.B., B.S.

*Assistant Surgeon in Charge, Civil Hospital,
Fatehjang, Attock District, Punjab*

I. K. was admitted into the hospital on 8th August, 1933, at 10 a.m. with two punctured wounds about $1\frac{1}{2}$ inches above the right eyebrow.

The wounds were quite close together, $\frac{1}{2} \times \frac{1}{2}$ of an inch in size and bone deep. The frontal portion of the skull was found fractured and depressed. There was an oedematous swelling round the injuries which occupied an area of $2\frac{1}{2}$ inches. Temperature on admission was normal and pulse 54; the pupils were dilated

and the right conjunctiva chemosed so that the cornea seemed to be lying in a trough. By the evening the swelling of the right eyebrow had extended to both the upper and lower right lids, and the patient was in his right senses.

The patient passed a very restless night; early on the morning of the next day I found him with pulse 40 and in a state of great irritation though the temperature was still normal, but the whole face had swollen and his talk was incoherent.

Operation.—An incision about 4 inches long was made just above the wounds and the skin reflected towards the face. A circular piece of bone $2\frac{1}{2}$ inches in diameter was found depressed.

A small portion of the healthy bone was trephined and removed. On elevating the depressed bone it was found fractured in three pieces. I removed two pieces and found a huge blood clot lying over the membranes of the brain. I removed the clot and washed the membranes with normal saline; in addition there were two linear fractures running upward and downward from the depressed piece. I left the largest of the three pieces of bone and closed the wound.

Next morning the patient was found to have regained his senses. Temperature was still almost normal and pulse 54, and the swelling of the face was subsiding.

For the following five days the patient had a raised temperature and severe pain in the head and he passed very restless nights.

On the night of the 15th the patient suddenly got irritation of the brain and ran out of the ward and after an hour or so he was brought under control.

Next morning the patient had a temperature of 101.6°F . with pulse 80 and he was very much depressed and out of his senses. His talk was quite incoherent and he complained of very severe stabbing pain in the head.

On the 17th I again opened up the wound and found the loose piece of bone I had left had fallen down and was pressing on the membranes and I removed it. For the following four days the patient was in a state of depression, regaining his senses at times but often indulging in meaningless talk. His pulse varied from 84 to 100 and his temperature from 102°F . and 103°F .

On the 22nd of August, the temperature was nearly normal and the patient was sleeping well and regained his senses.

The patient was discharged as cured on 12th September, 1933.

SUPPRESSED MENSTRUATION

By H. DASS, M.B., F.R.C.S. (Edin.)

Medical Officer, Jind City

A FEMALE patient, R. P., aged 15, came to the out-patient department of the Ranbir Hospital, Jind, early in 1931 with the complaint of weakness, pain in the lower part of the back and abdomen, and low fever. The pain had been present for two days and similar attacks of pain had been recurring periodically every month for a year and a half. The pain had been getting worse, each succeeding attack being more intense and lasting longer. At the onset the pain lasted for two days only, but this had increased to five days. The attacks of pain subsided but the weakness and low fever continued for about ten days longer.

* Rearranged by Editor.

Her temperature was 99°F. Her physical development was normal for her age, and there was nothing abnormal in her family history. She had never menstruated. In this part of the country, menstruation usually starts well before the age of fifteen. Suppressed menstruation was therefore considered in making a diagnosis. On abdominal inspection, nothing abnormal was seen, but, on palpation, a fairly tense round mass of the size of an orange was detected in the lower part of the abdomen in the middle line, apparently arising from the pelvis. It was slightly tender, and dull on percussion.

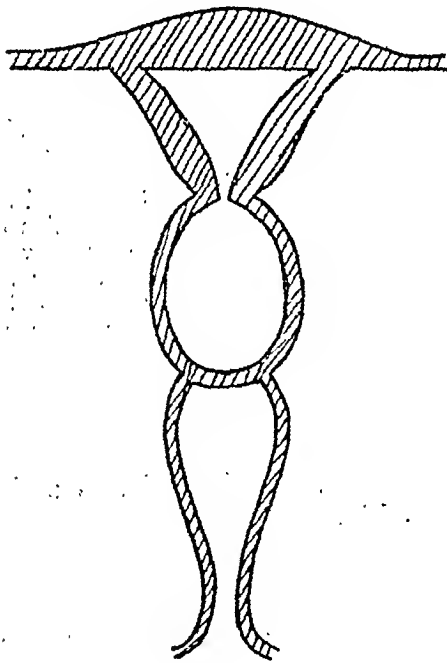
She was admitted as an in-patient, and on vaginal examination the hymen was found to be ruptured. No external os was visible in the vagina, the upper end of which was dome-shaped (diagram no. 1). No nipple-like projection, nor any aperture nor dimple could be seen at the usual site of the external os. Even a

of the abdomen over the site of the tumour did not help, but finally a thin dressing probe was arrested at a spot in the middle line, and when pressure was applied, it slipped upwards and a small stream of tarry blood came out past the probe. This opening was dilated very gradually at first with different sized probes, and then with uterine dilators (Hegar's) up to number 4. The tarry blood continued to escape and sixteen ounces were collected. The probes and dilators passed a distance of five inches into the uterus. Continuous pressure on the abdomen helped much in evacuating the fluid from the uterus.

After operation blood continued to escape for about six days, decreasing day by day in quantity and also changing in colour and consistency. The girl was discharged as cured after ten days.

She was again examined after two years and a half. She had been menstruating regularly

Diag. No 1.

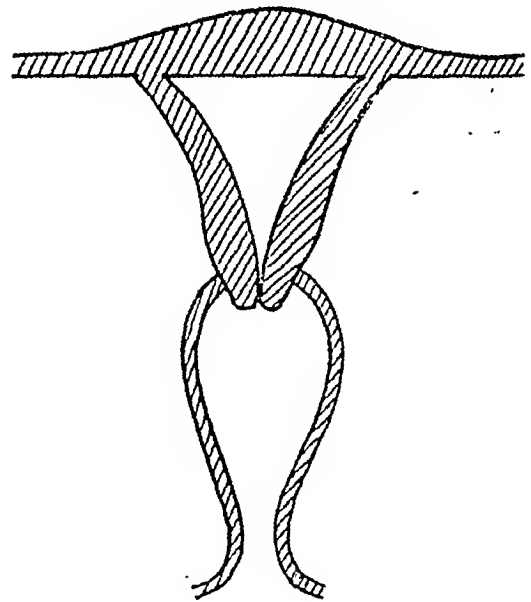


probe detected no opening. Bimanual examination showed that the site of the uterus was occupied by a mass, round and tense, of the size of an orange, tender and giving signs of fluctuation; no other abnormality could be detected in the pelvis.

She was advised to undergo an operation.

Under general anaesthesia with the patient in the lithotomy position the lateral walls of the vagina were retracted and a duck-bill speculum introduced. Nothing but the empty vault of the vagina was seen (diagram no. 1). At first the opening of the uterus was searched for in vain and even strong pressure on the lower part

Diag. No 2.



since the operation and had been feeling perfectly well in every way. Examination revealed a normally-formed external os of the usual shape and size (diagram no. 2). A uterine probe could not be inserted. She was again examined after a few days during menstruation, and the menstrual discharge was seen coming out of the external os, but the uterine probe could still not be inserted.

She was married about two months after the operation, and has not become pregnant yet. The question is whether she can conceive in her present condition, and, if not, will dilatation of the os help her?

Indian Medical Gazette

DECEMBER

ANÆSTHETICS IN INDIA

WE have not been able to trace the record of the first use of true anæsthetics in India—our most easily-available source of such information, the early numbers of this journal, only take us back to 1866—but we have little doubt that it was chloroform that was first used, and that this was introduced very soon after 1847, the year that the British gynaecologist, Sir James Simpson, first employed this anæsthetic. The immediate popularity that chloroform enjoyed has created the impression that it was the first drug introduced for producing general anæsthesia, whereas in actual fact both nitrous oxide and ether had been used for this purpose for some few years before Simpson made his great discovery, the latter anæsthetic actually by Simpson himself who abandoned it in favour of chloroform. Chloroform enjoyed a complete supremacy over its two predecessors, as an anæsthetic for major operations, for many years, but since the beginning of the century its popularity has been steadily waning and to-day in the large hospitals in Europe and America it has been almost entirely replaced by other anæsthetics, amongst which both ether and nitrous oxide figure very prominently.

The explanation of the increasing unpopularity of chloroform is that we are coming to realize more and more that it is not a safe drug. The reason it has taken the best part of a century for this fact to dawn upon the medical profession is not any innate stupidity on their part, but that the safety, or the reverse quality, of a drug, is a matter of comparison. One death due to chloroform in 2,600 operations will not strike the casual observer as a high mortality or as a justification for the appellation 'a dangerous drug', until he compares this with the death rates from ether and nitrous oxide anæsthesia, which even 20 years ago were placed at 1 in 8,000 and 1 in a million, respectively, by a reliable authority; that is to say chloroform is about three times as dangerous as ether and 400 times as dangerous as nitrous oxide. Whereas since its introduction little improvement has been effected in the chloroform itself or in the methods of giving it, there have been very marked advances in the technique of the administration of the other two anæsthetics. Another reason for this showing up of the dangers of chloroform anæsthesia is the improvement in surgical procedure and in the general operation mortality; at a time when the mortality was high an extra death or two, due to chloroform, did not attract much attention.

Furthermore, the safety of an anæsthetic is not the only consideration—though it should be the primary one—and the technically more skilled surgeon demands a corresponding advance in the efficiency of anæsthesia. It might, in fact, be said that the state of surgical advancement of an age, or of a country, was in inverse ratio to the amount of chloroform that was used in its major operations.

A quarter of a century ago some form of inhalation anæsthesia was considered the only possible procedure for major operations in most European and American surgical centres, and the three original anæsthetics—chloroform, ether and nitrous oxide—with the more recently-introduced ethyl chloride, still held the field, though the order of their popularity was being steadily reversed. But since this date there have been many advances; spinal anæsthesia was introduced, had a somewhat chequered early career, but has recently made steady progress; the practice of local and regional analgesia was improved and extended to major operations; and finally the rectal, oral and intravenous narcotics were experimented with and brought to a stage when they could be used with safety, to produce anæsthesia in man.

It cannot be said of the last group of drugs that they have yet reached the stage of perfection, because the variable factor—not in the drugs themselves but in the individual patient—makes the calculation of the *correct dosage* difficult, and necessitates the giving of doses insufficient to keep the patient completely 'under' for any length of time. However, these basal anæsthetics, as they are now called, have proved of immense value in reducing the amount of inhalation anæsthetic that it is necessary to give subsequently, and in abolishing psychic shock almost entirely. From the point of view of the patient this is one of the greatest advances that has been made since the original introduction of chloroform. Instead of having to undergo the terrifying experience of being wheeled to the theatre, meeting other corpse-like or vomiting patients returning to the ward, being frightened by white-clad figures and alarming-looking apparatus, and finally being suffocated into unconsciousness, the patient is given a rectal or intravenous injection, or is merely asked to swallow a draught, passes into unconsciousness in his own bed, and finally recovers to find himself in the same place and the operation over.

India is not usually slow to take advantage of medical advances, but the young surgeon coming to India to take up practice ten years ago must have been very surprised to find that in most hospitals, even in the large towns, chloroform was practically the only anæsthetic used. Some of the reasons for this have been discussed by one of our contributors in this number, so that we will not go into the matter in detail, but undoubtedly the main factor has

been the poverty of the country in general, and of medical institutions in particular. Some of the modern apparatus, for giving gas and oxygen, for example, is very expensive and beyond the means of all but the largest hospitals; hitherto nitrous oxide gas has had to be imported so that the cost for anything more than the amount necessary for short anaesthesia has been prohibitive for hospital use; and the large expenditure of ether entailed in the open method is a serious item. The climatic factor cannot be ignored, but except as far as expense is concerned it has been an excuse rather than a reason; but we do not feel justified in subscribing to Dr. Ganguli's suggestion that the leniency of the coroner is an important factor in determining the use of the most dangerous of anaesthetics.

However, the state of affairs that existed 10 years ago certainly does not exist to-day; as will be seen from a number of contributions that have appeared in this journal during the last year or so, and more particularly from those that will be found in this number, in many of the larger hospitals in India full advantage has been taken of the advances made in other countries, and chloroform is no longer the routine anaesthetic; we hope that the time is not far distant when the newer methods will be in general use even in the smaller hospitals

throughout the country. The excuses for the exclusive employment of chloroform in *mofussil* hospitals are no longer valid, as some of the best anaesthetic procedures do not entail the use of elaborate or expensive apparatus, nor of drugs of prohibitive cost. Furthermore, the choice of anaesthetic agents is a wide one, so that local prejudice—a very important factor and one which varies from district to district in India—can usually be countered; members of the stalwart races of the north, who object to losing consciousness, can be given spinal analgesics, whereas the more highly-strung resident of Bengal can be given a basal anaesthetic. Even here individual fancies can be met; some object to intravenous injections and can have nembutal by the mouth or paraldehyde by the rectum; others insist on them and can be given evipan.

We are publishing in this number of the *Gazette* four papers on anaesthetics by members of the staff of the Medical College Hospitals, Calcutta; two are written by surgeons and two by anaesthetists, and they all deal with the subject from the Indian point of view. No acute divergences of opinion are displayed and all the writers appear to us to support our contention that the use of chloroform in this country should be much more restricted than it is at present.

Special Articles

MODERN METHODS OF ANÆSTHESIA FROM THE SURGEON'S STANDPOINT

By W. L. HARNETT, C.I.E., M.A., M.D. (Cantab.),
F.R.C.S. (Eng.)

LIEUTENANT-COLONEL, I.M.S.

Professor of Surgery, Medical College, Calcutta, and
Surgeon to the College Hospitals

WHEN the writer came out to India in 1907 chloroform was the only anaesthetic available and was used for all purposes. It was supposed to be free from danger in a tropical climate on account of the rapidity of vaporization at high atmospheric temperatures, though whether this is so in the humid atmosphere of the monsoon months is open to doubt. Any advantages it may have possessed on this account were neutralized by the fact that the anaesthetic was usually administered by means of a Junker's inhaler with a vulcanite mask, so that it was practically a closed method, the percentage of chloroform in the inspired air being dependent on the vigour of the pumping and being quite unknown, probably tending to be on the high side. Everyone is familiar with the breath-holding which is produced by the administration of too strong a vapour to the still semi-conscious

patient, followed by struggling and deepening cyanosis, leading eventually to a few deep breaths which carry an unduly strong vapour into the lungs and may result in cessation of respiration, with dilated pupils, clammy dusky colour and a flickering, barely perceptible pulse. Another familiar picture is that of the sudden arrest of the heart's action from commencing the operation before the anaesthesia has reached the third stage, a phenomenon which Levy has demonstrated to be due to ventricular fibrillation, and particularly liable to occur when there is excess of adrenalin in the circulation. The consequent interruption of the proceedings until restorative measures have been successful is very disturbing to both surgeon and anaesthetist and is conducive to an atmosphere of subsequent anxiety which is not compatible with the best surgical work. Even if all goes smoothly the steady fall of blood pressure which takes place during a long operation and the action of chloroform as a protoplasmic poison are big factors in the production of delayed shock, and militate against the patient's chances of recovery. Many patients are lost owing to these causes, who might have been saved by the use of better anaesthetic methods,

the failure of the patient to rally from the operation and his death within a few hours being attributed to his disease and to the severe operation needed, and not to the true cause. For these reasons chloroform is regarded with disfavour by most surgeons except in a very limited class of cases. Nevertheless the comparative cheapness of the method, the simplicity and transportability of the apparatus and the apparent ease of administration cause it to be still regarded with favour in India. The following remarks of Professor Leonard Hill put the position very forcibly:—'Chloroform is a drug used by the young anæsthetist with the utmost hardihood and, until he has had the misfortune in his practice to meet with a death caused by it, he derides the dangers of the drug and asserts that its safety merely depends on the care and skill of the administrator. After losing his patient, he falls to dreading the unavoidable dangers of the drug, dangers which he is now the first to maintain cannot be met by any degree of skill in administration'.

In England in 1907 ether had to a great extent displaced chloroform as the anæsthetic of choice, but it was almost everywhere administered by the closed method with a Clover's inhaler, preceded usually by nitrous oxide gas, to avoid the irritating effects of the ether vapour in the early stages. This is a very efficient and safe method of anæsthesia, but it was never practicable in India, on account of the prohibitive cost of nitrous oxide gas. Closed ether without the preliminary nitrous oxide was used in some hospitals in India in the writer's experience with satisfactory results, though the induction stage was somewhat unpleasant for the patient. It is little more expensive than chloroform as the amount of ether used is small, 4 to 6 ounces sufficing for most operations, it is speedy in action and powerful enough to overcome the most refractory patient. On the other hand the anæsthesia is not very satisfactory especially for abdominal work, as the respiratory movements are very deep from the anoxæmia, relaxation is imperfect leading to difficulty in intra-abdominal manipulations and in closing the abdomen, post-anæsthetic vomiting is worse, and the incidence of pulmonary complications is high. Ethyl chloride may be used in place of nitrous oxide gas for the induction, but is apt to be followed by troublesome vomiting and does not appear to have been much used in India.

Closed ether has now been almost entirely superseded by the open method, in which the air supply is in no way restricted and which requires no more complicated apparatus than is necessary for the administration of chloroform on the open mask. The working margin of safety is much wider than in the case of chloroform, as 16 per cent to 18 per cent of ether in the inspired air is necessary for induction as against 2 per cent to 3 per cent of chloroform. This

involves the use of a large amount of ether, but it may be considerably reduced by the preliminary injection of morphine gr. 1/6 with atropine gr. 1/100, the latter to check the tendency to salivation which is such a troublesome feature of ether anæsthesia. In febrile and toxic cases this is an ideal method, the patient is in a drowsy condition by the time he reaches the theatre, induction is easy and pleasant, the anæsthesia is perfect and there is little vomiting or after-effect. In healthy subjects it may be difficult to induce anæsthesia by this method without the expenditure of considerable time and a large amount of ether, and in such cases it is best to induce by a mixture of chloroform and ether, changing over to ether alone as soon as full anæsthesia is attained. Pure chloroform should not be used for induction if a preliminary injection of morphine and atropine has been given, as this combination causes severe respiratory depression. This is a most excellent and safe method for routine work and in its use the unpleasant accidents referred to above as common with chloroform are never met with, but it has the drawback that in hot climates very large quantities of ether are needed, 12 ounces to one pound for major abdominal procedures. It must also be remembered that in long operations ether has the same action as chloroform, causing a fall of blood pressure and depression of respiration; furthermore its irritating action on the respiratory mucous membranes involves an increased risk of pulmonary complications, only partly checked by the preliminary injection of atropine. In Europe the use of warmed ether vapour is adopted by many anæsthetists to counteract the chilling effects of the cold vapour on the lung alveoli, but the apparatus is complicated and in this climate is hardly necessary. For thoracic surgery and in mouth cases the endotracheal administration of warmed ether vapour under pressure by means of a catheter passed through the larynx has replaced all other methods; the patient is first anæsthetized in the ordinary way, then by the aid of a direct-vision laryngoscope the catheter is passed down to the bifurcation of the trachea and the supply of warmed ether vapour maintained by a bellows or preferably by an electric pump. The complexity of the apparatus and the skill required to pass the catheter have so far prevented this method being taken up in India. For thyroid and neck cases there is no better method than the rectal administration of a mixture of 75 per cent ether and 25 per cent olive oil (the percentage of ether should be less in young subjects), 1 ounce to each 20 pounds of body-weight up to a maximum of 8 ounces, preceded by morphine atropine injection. The patient is put to sleep in bed and is ready for operation in about 20 minutes; should the anæsthesia be light it can be deepened by a little open ether; in mouth operations the fact that the cough reflex is lost is a drawback,

necessitating careful swabbing to ensure that no blood enters the trachea.

During the last few years a great advance has been made in the technique of inhalation anaesthesia by the introduction of basal anaesthetics. These are substances that are administered to the patient before operation, depriving him of consciousness, so that he loses all sense of apprehension and knows nothing of the journey to the theatre or of the preparations for the operation. He wakes up some hours later, with the intervening period a complete blank and by that time post-operative shock and vomiting should have passed off. The value of all this in the case of nervous patients, of whom we have many in India, cannot be over-rated, and in addition these drugs have an even more important action in that they reduce the amount of the main anaesthetic agent that is needed to less than half, thus doing away with one of the chief objections to the open ether method of anaesthesia. These drugs fall into three chief groups:—

(a) *Paraldehyde*.—This is the writer's favourite for all abdominal work. A preliminary injection of atropine gr. 1/100 is given and, about three-quarters of an hour before operation, paraldehyde, 1 drachm per stone of weight up to a maximum of 10 drachms in 10 times its bulk of saline, is run into the rectum, which should be cleared by an enema 3 or 4 hours before. It is important that the paraldehyde be fresh, otherwise acetic acid may have been formed by decomposition, which will irritate the rectum and lead to its rejection. A dose of veronal overnight helps greatly. A deep sleep will be produced and only about 6 to 7 ounces of ether are needed for a cholecystectomy or gastro-enterostomy. Children take this drug very well. The only ill-effect is that patients, especially if alcoholic, may be boisterous and excited for some hours afterwards. The anaesthesia from the surgeon's point of view is perfect with excellent relaxation, and the method is of wide applicability.

(b) *Avertin (tribrom-methyl alcohol)* is also used by rectal injection, the dose being 0.1 gramme per kilogramme of body-weight, diluted in saline. Its effect is similar to that of paraldehyde, but its narcotic action is more profound and relaxation more perfect, there is a tendency to a fall of blood pressure and so the margin of safety is narrower. The amount of ether necessary after avertin is smaller than in the case of paraldehyde, about 4 ounces sufficing for most purposes and it must be admitted that the anaesthesia is more perfect, but against this must be set its high cost, about three to four rupees per dose (according to dosage) as against three annas per dose of paraldehyde.

(c) *The barbiturates* of which nembutal and pernocton are the most used. I have only experience of nembutal, which I frequently use in doses of $4\frac{1}{2}$ grains orally as a preliminary to

operations under local anaesthesia by regional or nerve block. Patients hardly notice the needle pricks and with this aid the scope for local anaesthesia in India is much enlarged, as by putting the patient to sleep it obviates the principal objection to these methods. It may be given intravenously or orally, the results with the former method being better, as the more exact dosage reduces the amount of the main anaesthetic necessary. When it is given orally the rate of absorption varies and therefore so does the time taken to put the patient to sleep. The sedative effect lasts 1 to 5 hours and there is complete amnesia for the whole period.

Sodium evipan is the latest addition to this series. It is given by intravenous injection, the dose being graduated according to the effects observed during injection of the first 4 c.cm. It gives complete analgesia commencing within a minute and lasting about 20 minutes. It is admirable for short operations not requiring perfect relaxation and we have found it useful for putting Kirschner wires through the tibia or os calcis, and in setting up fractures of the femur or tibia and fibula. By the time the patient comes round the limb is slung up in the skeleton splint with the extension in action, the absence of relaxation not being of much importance where skeletal traction is to be employed, though it renders the method unsuitable for putting up fractures in plaster-of-Paris, where the position must be perfect before the cast is applied.

Nitrous oxide and oxygen anaesthesia was developed during the war. It is of immense value in patients suffering from severe shock or acute sepsis, on account of the lack of toxic properties in the agents employed and the rapidity of elimination. For these reasons it is the anaesthetic of choice in many acute abdominal cases and in diabetics suffering from surgical complications, both classes of patient who are peculiarly susceptible to the poisonous action of ether and chloroform. It has serious drawbacks however, the heavy bulky plant, the necessity of an expert anaesthetist and the enormous cost of the nitrous oxide in this country. In abdominal surgery it is not satisfactory on account of the imperfect relaxation but this can be counteracted by the preliminary use of basal narcotics. My personal practice is to reserve it for use in diabetic cases and in acute abdominal cases that are bad risks.

Cost.—The comparative cost of the methods described above works out as follows at the ordinary Calcutta prices of the drugs used, though of course they would be cheaper in the case of hospitals that obtained them from the Medical Stores or through a 'home indent'.

1. Morphine, atropine, and ether
say 1 pound .. Rs. 3-8
2. Paraldehyde 1 ounce and
ether, say, 6 or 7 ounces Re. 1-11

(Continued at foot of opposite page)

THE CHOICE OF A GENERAL ANÆSTHETIC IN MAJOR OPERATIONS IN INDIA

By M. C. GANGULI, M.B.

Anæsthetist, Medical College Hospitals, Calcutta

Up to the beginning of the last decade the selection of an anæsthetic in India was a matter of 'Hobson's choice', because chloroform was practically the only anæsthetic used; the words chloroform and anæsthetic were almost synonyms, and the anæsthetist was often known as the 'chloroformist' by the profession as well as by the general public.

It would perhaps be out of place to give all the reasons why chloroform has maintained its popularity in this country; suffice it to say that the two main ones are the ease with which it can be administered and its cheapness. Furthermore, it has hitherto been the exception in this country for any thorough enquiry to be made by the authorities into a case of death during anæsthesia. The consequence has been that any person—qualified or not—has been able to style himself an anæsthetist and to administer chloroform; the amount of skill required for this is minimal, and the risk was entirely borne by the unfortunate patient.

Fortunately the times are changing for the better and, at least in the teaching hospitals in India, the number of which are gradually increasing, almost all recognized methods of anæsthesia are practised and the absolute supremacy of chloroform has been undermined.

The choice of anæsthetic has to be made from several points of view, those of the patient, of the surgeon and of the anæsthetist, independently and conjointly.

(Continued from previous page)

3. Avertin 7 c.cm. and ether
4 ounces Rs. 4-14
4. Nembutal $4\frac{1}{2}$ grs. and ether
6 ounces Re. 1-14

Spinal anæsthesia

As this forms the subject of another paper in this issue I do not propose to deal with it. Its utility in the surgery of the lower half of the body has long been recognized and for some time I have employed the method used at St. Mark's Hospital for rectal work. Half a c.cm. of 10 per cent stovaine in normal saline is injected with the patient sitting up until the anæsthesia begins to develop, when he lies down. The result is anæsthesia of the rectum, perineum and neighbouring parts without paralysis of the legs; the relaxation of the anal sphincter is perfect. The latest development is the use of perein for the production of anæsthesia extending high enough for abdominal work. I have been much impressed by the few cases I have so far seen and I foresee a great future for this method, especially when combined with a basal narcotic.

The patient wants an anæsthetic which will imperceptibly put him under its effects, and that rapidly, without the knowledge and terror of going under an anæsthetic. He must not have the slightest misgiving about the safety of the procedure, not only as regards his life, but also as regards the feeling of pain. In other words the patient should not have the least degree of psychic shock, and lastly he wants to be absolutely free from post-anæsthetic troubles.

The surgeon can only be at his best when there is complete relaxation of the field of operation and of the whole muscular system, when the heart is beating regularly, the blood is a bright red colour, and the anæsthetist quite free from anxiety.

The desire of the anæsthetist is not different from that of the patient and the surgeon, but in addition he wants the anæsthetic to be easy of administration.

Have we such an anæsthetic? Unfortunately to-day the answer is in the negative. We have no single anæsthetic which is ideal and will fully satisfy all, but with a proper combination of different anæsthetics, with a skilled administrator, and an appreciative and light-handed surgeon one can almost reach the ideal desired.

For many years morphine and scopolamine were the only drugs used to lull the patient's fears and abolish his excitability before the actual administration of an anæsthetic, and since the experiments of Crile showed that pre-medication by morphine prevents shock to an appreciable degree it has been used with much greater frequency. But the quest for a better pre-mediator went on as it was found that morphine and scopolamine did not sufficiently reduce the total amount of anæsthetic required during an operation, with its attendant risks. The results have been encouraging. To-day we have several pre-anæsthetics which also act as basal narcotics or sub-anæsthetics. They are so called because by their use the quantity of actual anæsthetic required to maintain anæsthesia can be reduced to an amazingly small amount.

Ether, avertin and paraldehyde by the rectal route in the proper dose, administered by the attending nurse in the ward, put the patient to sleep in his own bed and he does not know just what is going to happen. He is carried in his sleep to the operating theatre where the operation is performed in comfort, with very little inhalation anæsthesia or local infiltration. The patient is returned to his bed and wakes up from a fairly long sleep hardly believing that the whole thing is over. More recently we have still other basal narcotics wherewith to achieve the same end—the barbiturates, e.g., pernocton, amyral and nembutal. They may be used intravenously or by the mouth.

Regarding safety, it must be confessed that there is no anæsthetic or even sub-anæsthetic

which ensures cent per cent safety. Drugs introduced into the system by parenteral injection or by the mouth are uncontrollable, because a dose calculated to be appropriate for a certain patient may prove an over-dose and the excess can neither be withdrawn nor efficiently combated; furthermore, as the elimination of injected drugs is slow, troublesome or even fatal consequences may ensue. The idiosyncrasy to morphine is almost proverbial and the behaviour of scopolamine is wayward, as in some cases instead of the expected depression of the cerebrum it may actually excite it. The safe dose of the barbiturates has not yet been worked out to full satisfaction. The minimum effective dose should be given by the intravenous route. By the mouth or by the rectum they can also be given, but their action is delayed and the dose is difficult to regulate. They are very toxic—nembutal and pernocton being twice as toxic as the sodium amytal. The rectal injections also are not completely controllable, but they are partially controllable, as an excess can be withdrawn from the rectum unless some has escaped into the upper parts of the gut by retro-peristalsis. Avertin is perhaps more toxic than ether and ether more than paraldehyde, though at the same time their anæsthetic properties are in proportion to their toxicity.

The verdict against chloroform as the most dangerous drug has been passed by a consensus of opinion. Ether is decidedly safer and nitrous oxide with oxygen the safest, ethylene standing midway between the two.

Unfortunately with the great majority of anæsthetics post-anæsthetic complications cannot be completely avoided. With gas and oxygen, however, lung complications do not occur and vomiting is rarely seen. With ether and chloroform, vomiting and pulmonary complications are often distressing the latter trouble being more common with ether, but, with a progressive knowledge of better pre-operative preparation, improved methods of anæsthesia and pulmonary ventilation, the post-anæsthetic complications have been reduced to a minimum. By avoiding dehydration due to starvation and excessive purgation and by increasing the glycogen reserve with glucose and by alkalization, the acidosis is greatly lessened and the patient bears the post-operative period in much less discomfort. By attending to the infective foci in the mouth, by diminishing secretions with a preliminary injection of atropine, by warming the anæsthetic vapours, by avoiding all shock-producing factors, and by adequate ventilation of the lungs with inhalation of carbon dioxide and oxygen, during and after the operation, pulmonary congestion, post-operative atelectasis and pneumonia have become rare. The patient is also rapidly de-anæsthetized by increasing the pulmonary ventilation with carbon dioxide, and the drugs,

acting on the organs for a minimum period, hardly affect them adversely.

Complete relaxation of the field of operation and the whole muscular system is essential, not only for the surgeon to operate in comfort, but also for the prevention of shock and the success of the operation as a whole. Greatest relaxation is obtained by chloroform, less by ether and least by nitrous oxide and oxygen; but relaxation with chloroform is obtained at the sacrifice of safety, because, it has been calculated, the difference between the percentage of chloroform in the blood required to obtain complete narcosis with relaxation and the lethal dose is very small, and consequently, even with long experience, extreme vigilance is absolutely essential to prevent a catastrophe. With ether an adequate relaxation can always be attained with a fair margin of safety, and as the respiration and circulation are stimulated by it the colour of the blood is kept very satisfactory. Though gas and oxygen is the safest of them all the relaxation it gives is quite insufficient for most abdominal operations.

To get access to the organs during an operation the surgeon has often to compete with the muscles of the abdomen, and the struggle that ensues produces a degree of shock for which the safety of the gas can hardly compensate, and a 'safe' anæsthetic becomes dangerous, due to its inefficiency.

The anæsthetist can be free from anxiety only when he knows his work. He must be thoroughly familiar with the dangers, defects and the action of the agent he is using, the requirements of the operation, and with the peculiarities of the surgeon. To enable the anæsthetist to work at his ease the surgeon must not only know him, but also the limitations of the anæsthetics used. There must be a thorough understanding between the surgeon and the anæsthetist for a smooth-sailing operation. There are times when the 'surgeon has to unbend and the anæsthetist rise to the occasion'.

As regards easy administration of an anæsthetic it may be mentioned that the greater the skill the anæsthetist acquires the easier the administration becomes. Paradoxical though it may seem, usually the safer anæsthetics require greater skill than the less safe ones, and in this apparent ease in the administration of the latter lies one of their dangers, because, as I have already said, anyone feels himself competent to administer them.

It will appear now that we possess very satisfactory pre-anæsthetics and though the means to prevent post-anæsthetic complications have been greatly improved there is still room for advance. The two factors with which one is most concerned is the safety and efficiency of an anæsthetic. Our safest anæsthetic is not the most efficient nor is the most efficient the least

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SPINAL ANALGESIA*

By J. C. DRUMMOND, M.Ch., M.B. (Liv.),

F.R.C.S. (Edin.)

CAPTAIN, I.M.S.

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THE reduction in the mortality rate of extensive operative procedures which has followed upon recent anæsthetic developments has brought a realization that our two old stock anæsthetics, chloroform and ether, are greater tissue poisons than we had previously thought. Until research produces a more ideal inhalant they will still be necessary, but the present tendency is to restrict their use to a minimum,

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safe. But it must be realized that though safety is our primary concern it is not the sole concern. The operation has to be done and that successfully. So one has to strike a middle course and select a combination of anæsthetics which will not be unpleasant to the patient, and at the same time ensure the maximum of efficiency with safety.

With an injection of morphine and hyoscine, or the administration of an actual basal narcotic—preferably rectal paraldehyde—the induction with ether with its smell and irritation is rarely unpleasant and often not objected to by the patient at all. Induction of anæsthesia with nitrous oxide and oxygen after pre-medication, and maintenance by it with additional ether, when required for satisfactory relaxation, is least disagreeable to the patient, safe in the extreme, and efficient to the maximum, with post-anæsthetic sequelæ reduced to the minimum. The difficulty with nitrous oxide in this country is its high price and that it requires a rather expensive machine and a skilled anæsthetist. So it is usually not available except for the lucky few and its place has to be taken by the less desirable ether in the large majority of cases; or some other method—local or spinal—has to be combined with basal narcosis.

The selection of an anæsthetic or combination of anæsthetics in patients of different age and physique, and in different pathological conditions, is a matter which requires careful consideration, but which it is not the purpose of this paper to discuss.

In conclusion, it may be stated that there is no single anæsthetic which will meet all requirements. To do the best for the patient an anæsthetist must be familiar with all the methods of administration, so that he may choose the right anæsthetics suitable to the particular case, and 'as an artist becomes skilful in mixing his colours, so must the anæsthetist become skilful in arranging his anæsthetic sequences'.

or, in certain cases, to dispense with them altogether. Among the newer methods which have come into use, intrathecal analgesia has made a reappearance in an entirely new guise, shorn of most of its previous disadvantages and with newly acquired merits.

HISTORICAL

The subject dates back to the work of Corning in 1888. The earlier results were, on the whole, disappointing. The drugs used were unsuitable, the diffusion and gravitation of solutions in the subarachnoid space were not properly understood, the technique imperfect and the wrong type of case was frequently selected for its application. A revival of popularity followed the introduction of stovaine, limited controllability having been attained by making the solution hyper-baric, i.e., heavier than cerebrospinal fluid, by the addition of glucose. This, however, never seriously competed with the older anæsthetics for routine use, and the majority of surgeons gave it up altogether.

In 1928 a tremendous impetus was given to the subject by the work of Dr. George P. Pitkin of New Jersey which resulted in the preparation known as spinocaine and the technique with which it is employed. In the December issue of the *American Journal of Surgery* for that year no fewer than fourteen articles appeared on the subject, and, for the first time, spinal analgesia began to be used on an extensive scale. The following year saw the introduction of a new drug, perein, chemically unrelated to the novocaine group and possessing characteristics especially suitable to intrathecal analgesia. This drug lends itself so well to surgery of the upper abdomen that many surgeons now use it as a routine in such operations.

ADVANTAGES OF SPINAL ANALGESIA

1. The absence of the secondary devitalizing effects of prolonged anæsthesia with ether or chloroform, leading to quicker post-operative recovery.
2. No post-anæsthetic strain trauma due to vomiting and coughing.
3. Rarity of pulmonary complications. This is specially valuable in India, where pulmonary complications are commoner than in Europe.
4. Food may be taken early, and will be digested and assimilated.
5. In some cases a patient may be permitted to suck toffee or drink an egg flip while the operation is actually in progress.
6. It is effective in strong subjects and in alcoholics. For patients who come into both these categories, it is perhaps the only satisfactory anæsthetic.
7. It provides incomparable muscular relaxation.
8. Better surgical exposure in abdominal operations is allowed. This is partly due to the

* From a paper read at a meeting of the Calcutta Branch of the British Medical Association, 10th November, 1933.

absolute relaxation and partly to the collapse of the intestines which is produced by paralysis of the inhibitory fibres of the sympathetic. This leads to less rough handling of the viscera or dragging on the mesentery and to more facile and quicker operative technique. It is possible to work through a smaller incision.

8. In out-stations, where no skilled anaesthetist is available, it facilitates the performance of operations which could not otherwise be safely undertaken. Needless to say, it is not advisable to dispense with the anaesthetist if one is available.

9. The apparatus is simple, portable and cheap.

10. Some patients prefer it.

It will now be convenient to deal briefly with the three drugs which have been chiefly used in the production of spinal analgesia—stovaine, novocaine and percaine.

STOVAINE

This is employed in 5 per cent or 10 per cent solution rendered hyper-baric by the addition of glucose. Half to 2 c.cm. are injected in the lumbar region with the patient in the sitting position, the solution descending to the lower part of the spinal canal by the action of gravity. The action is somewhat uncertain and analgesia above the umbilicus cannot be obtained by this method in safe dosage. The fall in blood pressure is severe, because of the toxic nature of the drug, the high concentration in which it is employed, and the absence of a viscid vehicle to slow down the rate of absorption and assist evenness of diffusion. Unpleasant sequelae frequently follow its use,—*e.g.*, severe headache, urinary incontinence or spasm of the vesical sphincter, paralysis of the sixth cranial nerve and even degenerative changes in the cord (Spielman). In the past it has been frequently used on patients suffering from shock or in too devitalized a condition to stand a general anaesthetic, in fact on the type of patient least suited to spinal analgesia. It is scarcely to be wondered at that it never came into universal use and that it is now practically obsolete.

Following the introduction of spinocaine, I applied stovaine to the Pitkin technique, in more dilute solution, rendered hypo-baric. Though satisfactory analgesia of the upper abdomen was obtained, many of the disadvantages of the drug were still present and I have never felt at ease while using it. In the past it has enabled me to operate where no skilled anaesthetist has been available, but I think that its use now is unjustifiable and that it should be relegated to the realm of the medical historian.

SPINOCAINE

The active principle is novocaine, the toxicity of which is not high. The objections to intrathecal novocaine that previously existed were

(1) the transitory nature of the analgesia, (2) the lack of control of the height and extent of the analgesia, and (3) the serious drop that occurs in the blood pressure. The formula and technique of using spinocaine was devised by Dr. Pitkin with the object of negating all these in the following manner:—

1. The transitory nature of the analgesia is corrected by addition of a viscid substance, gliadin, which delays absorption and prolongs the effect to about one and a half hours. It also assists to even out the diffusion and prevent toxic symptoms due to too rapid absorption of the novocaine.

2. Controllability is achieved by rendering the solution hypo-baric by the addition of alcohol so that it floats on the cerebrospinal fluid 'like an air bubble in a spirit level'. The injection is made in the upper lumbar region with the patient lying on his side, the head being lower than the spine. The attitude may be varied so that the part of the cord to be anaesthetized is uppermost and the height of the analgesia may be controlled by placing the patient in varying degrees of the Trendelenberg position.

3. The drop in blood pressure is controlled by the addition of strychnine to the solution and by the preliminary injection of ephedrine-adrenalin. The latter is given together with a local anaesthetic used to anaesthetize the site of the spinal injection.

The success of spinocaine may be gauged by the extent it has been used. Many surgeons in America employ it on every possible occasion, even for operations on the breast. Strauss, in his joint statistics of 83,698 cases, calculated a mortality of 0.016 per cent, or one death in every 5,978 cases. Carre and Borchard stated that they expected three immediate and three remote deaths in every 10,000 cases. It must be remembered, however, that these are the figures of experts; mishaps which occur in the hands of the occasional operator are a little apt not to be recorded.

In practice, though excellent results can be obtained with spinocaine, it is sometimes wayward in action and does not always behave like the bubble in the spirit level. The alcohol in the solution may mix with the cerebrospinal fluid, precipitating the heavier constituents to the action of gravity. Further, it is based on a normal specific gravity of the cerebrospinal fluid of 1007, but this is subject to fairly wide variations—between 1003 and 1010. Like stovaine, it is given in concentrated solution, and, in spite of the viscid substance added, ocular palsies and other unpleasant symptoms have been observed. It must be admitted that in spite of careful technique small quantities of spinal analgesic solutions are liable to reach a higher level than intended, and it follows that no concentrated solution can be really safe.

I still use spinocaine for inguinal herniotomy, where small dosage suffices and absolute relaxation and prolonged action are not required, but I have given it up in favour of percaine for high abdominal analgesia.

PERCAINE

This is a quinine derivative having no chemical relationship to any other local anæsthetic. It is used in extreme dilution, being weight for weight easily the most powerful local anæsthetic known. In the spinal theca 7.5 milligrammes of percaine will produce an analgesia more intense and considerably more prolonged than 150 milligrammes of novocaine. The dilution of effective solutions is so extreme that the weight of the drug adds practically nothing to the specific gravity of the solvent and makes it unnecessary to resort to the addition of alcohol to produce a hypo-baric solution. When sufficiently diluted it exerts a selective action on the anterior roots of the dorsal nerves, giving the absolute relaxation of the muscles of the abdominal wall which is so characteristic of the drug, while having no appreciable effect on the phrenics or vital centres of the medulla, in normal dosage. No cases of ocular palsies have been recorded. In dilutions of 1 in 1,500, or greater, it can be injected in comparatively large bulk (20 c.cms.), leading to more uniform certainty of action. Post-anæsthetic headache is rare and the fall in blood pressure is relatively small and readily controlled with ephedrine. No cases of vesical incontinence or irritability have been recorded. Constipation for two or three days has been noticed in cases in which the mesentery has been pulled on, but this is probably true with all anæsthetics. There is, however, one disadvantage. As the maximum effect is on the anterior roots of the dorsal nerves some or all of the intercostal muscles are put out of action. If analgesia is obtained to a high level, respiration may be dependent on the phrenics. In practice, this does not matter if oxygen be available.

PSYCHIC CONSIDERATIONS

Though spinal anæsthesia may be safe and ideal from the point of view of the surgeon, it may not be satisfactory to a nervous and highly-strung patient. The avoidance of psychic shock is important. If the patient is at all apprehensive, morphia may be given an hour before operation and the ears plugged with cotton-wool. The combination of avertin and percaine has been advocated, but the use of any drug which masks the action of the spinal analgesic is undesirable. I find that a minimum dosage of percaine combined with open ether is very satisfactory in nervous cases. The ether is not administered until after the action of the percaine has been ascertained, and it is surprising how little need be given.

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BASAL ANÆSTHESIA*

By PROFULLA KUMAR MUKHERJEE, M.B.

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A BASAL anæsthetic is one which acts as a base for the administration of some other form of anæsthesia or analgesia, thereby reducing the amount of anæsthetizing agent required and minimizing the insult to the tissues caused by this agent. It is needless to point out the advantages to be gained in prolonged and difficult surgical operations by restricting to a minimum the amount of chloroform or ether used. The striking decrease which has been accomplished in the mortality rates of severe surgical procedures by the employment of modern anæsthetic methods is now well known.

Even if research were to produce a non-toxic inhalation anæsthetic, free from the unpleasant features of chloroform and ether, basal anæsthesia would still retain a position amongst the agents at our disposal by reason of an inherent virtue not possessed to any appreciable extent by any other method. I refer to the avoidance of psychic trauma, or, as Crile puts it, 'anoci-association'. By its use a nervous patient may swallow a tablet or have an injection in the ward and pass into a deep sleep before he enters the operating theatre. When he wakes up again, he is back in the ward with his operation over. He is spared the apprehensive journey from the ward to the theatre, the suspense of waiting for his turn and the sight of

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SELECTION OF CASE

A few years ago the attitude frequently taken towards spinal analgesia was 'this patient won't stand a general anæsthetic; let's give him a spinal'. It is now realized that the patient who is shocked or devitalized by some toxic condition or wasting disease is not a suitable subject. Regional analgesia offers a safer alternative in these cases. There are some who go so far as to say that spinal analgesia should never be used on a bad risk case, but there are some bad risks in which absolute relaxation is essential to the safe conduct of the operation, intestinal obstruction for example. The recent acute abdomen in a fairly robust individual is not considered to be a bad risk. A change has also taken place in the type of operation in which spinal analgesia is most commonly employed. Previously used for operations on the pelvis and lower limbs, it has become mainly an abdominal anæsthetic, particularly for extensive resections and operations where wide exposure is required.

* Paper read at a Clinical Meeting of the British Medical Association, Calcutta Branch, on the 10th November, 1933.

white-robed figures and instrument cabinets. Post-operative neuroses are avoided, the mental outlook of the patient less disturbed and convalescence accelerated.

Drugs employed

The chemist is producing new drugs for basal anaesthesia faster than the clinician can test them. It can safely be predicted that still more perfect drugs will be available in a few years time. Those now in most common use are :—

- (1) Derivatives of barbituric acid.
- (2) Avertin.
- (3) Paraldehyde.

1. Since the introduction of veronal thirty years ago many derivatives of barbituric acid have been produced. They may be roughly divided into two groups—those that are relatively non-toxic, are slow in absorption and have prolonged action, and those that are more toxic, are rapidly absorbed and have a shorter action. The ones that have given satisfactory results are nembutal, evipan sodium, and pernocton, and amongst these nembutal in my hands proved to be of special advantage.

Nembutal.—Though this can either be given intravenously or by the mouth, oral administration has been the method of choice and in Indian patients doses of $4\frac{1}{2}$ grains for males and 3 grains for females have been used. Sleep follows in about half an hour. Corneal reflex is maintained, as is the cough reflex. The additional anaesthetic used in this series has usually been 1 per cent novocaine solution either as an infiltration or as a nerve block and this procedure has invariably proved of extreme advantage in cases of operations on the jaw inasmuch as the patient has been quiet, subconscious and unconcerned, yet whatever trickled into the throat has been thrown out by the patient. No late toxic effects have been noticed.

Evipan sodium.—The solution is freshly made in 10 c.cm. of triple distilled water which is supplied by the maker in a separate ampoule and 4 c.cm. of the mixture is injected intravenously at the rate of 0.5 c.cm. per half a minute and the muscular relaxation, as evidenced from observation of the masseter, is used as the guide to subsequent dosage. The injection may, if necessary, be continued up to a maximum of 10 c.cm. until the desired depth of anaesthesia is obtained. The anaesthesia it yields is somewhat transient and variable, the relaxation is imperfect, and thus its value is confined to short operations where relaxation is not required. Alcoholics get boisterous; some are susceptible and the respiration is often depressed, and in one case it went down to three.

Pernocton.—It is obtained in ampoules. The dose is calculated from body-weight—0.5 c.cm. for every stone of body-weight with 0.5 c.cm. added to the total; this is injected

into the vein at the rate of 0.25 c.cm. per quarter minute.

The drug is inefficacious on alcoholics and some non-alcoholics also remain wide awake. The quantity of inhalation anaesthetic required is not appreciably diminished. Post-operative morphia is required in every case.

2. *Avertin.*—Avertin is tri-brom-methyl alcohol and is available both in crystals and fluid form. The latter is more convenient to measure, but slightly more expensive. It is a somewhat unstable drug and must be tested for decomposition before use. This is done by the addition of a few drops of Congo red solution, 1 in 1,000, before administration. If the indicator does not change its colour, the solution is safe for use. In actual practice, no trouble has been experienced by decomposition of the solution.

It is administered by the rectal route, the dose being calculated by body-weight, 0.1 c.cm. of fluid avertin per kilogramme of body-weight. The avertin is diluted, or rather emulsified, in forty times its bulk of distilled water roughly at body temperature and slowly instilled into the rectum. A simultaneous injection of hyoscine compound is given. The patient falls into a deep sleep a few minutes after the completion of the rectal instillation and is ready for removal to the theatre. During this stage it is advisable not to have the patients disturbed, as for example, by being examined by students. Open ether may be administered without risk of waking the patient. His heart is not weakened by his fighting and struggling in the second stage, and muscular relaxation is obtained with a comparatively trifling dose of inhalation anaesthetic. The slow, easy, natural type of respiration is reassuring both to surgeon and anaesthetist. The patient returns to the ward still asleep, unlikely to be troubled with vomiting and the trauma of straining after operation, or to contract pulmonary or gastro-intestinal complications.

Avertin has been used in 65 selected cases of major operations with satisfaction to the surgeon, the patient and myself. Compared with other basal anaesthetics, its main disadvantage lies in its cost. As already indicated, its instability has not been found to be a disadvantage in actual practice. It is fairly sure in action, sleep is early and deep, and it contributes to relaxation to a greater extent than any other basal narcotic, therefore less inhalation is required to complete the anaesthesia.

In calculating the dose it has been found that 5 c.cm. of avertin is sufficient; weight due to superfluous fat should be neglected in estimating the dose. With larger doses slight cyanosis often prevails. One disadvantage however is that the blood pressure falls 10 to 20 mm. of Hg. within the first fifteen to thirty minutes.

The drug has been used in conjunction with ether in most cases, with novocaine infiltration in three cases of tumour of the thyroid, two

cases of cancer of the breast (total removal) and one case of tumour of the jaw, and with spinoecaine in three cases of acute abdomen. It is a bad risk with spinoecaine as both of these drugs reduce the blood pressure. This may, however, be counteracted by the combined use of ephedrin and adrenalin.

Of the 53 cases done with ether, slight congestion of the lungs at the base developed in four and there was troublesome vomiting in three gastro-jejunostomy cases.

In one case of cancer of the breast done with avertin and ether the patient died of sudden heart failure 10 days after operation when the stitches had been removed from a perfectly clean healing wound. After death the family doctor gave a history of the patient having had heart attacks. The blood pressure before operation was 120 systolic and 70 diastolic. Autopsy was not allowed.

In one case of cancer of the breast done with avertin and novocaine infiltration the patient died five days after operation with symptoms of ileus starting from the second day after operation. The patient was aged 60 and weighed 22 stone; the systolic blood pressure was 130, diastolic—70. Only 5 c.cm. of avertin and a 0.5 per cent solution of novocaine were used.

No other trouble was encountered in the whole series.

3. *Paraldehyde*.—The drug must be chemically pure, otherwise it gives rise to an irritative colitis.

The dose is calculated from the body-weight, one drachm for each stone, the limit being fixed at one ounce. This is diluted twelve times in normal saline. Seven and a half grains of veronal are given overnight; atropin 1/100th grain is injected and then the solution is slowly instilled per rectum. The patient falls asleep in about half an hour. In a series of one hundred cases in which this form of anæsthesia was used, congestion at the base of the lungs appeared in only two and troublesome post-operative vomiting was not noticed in any. A comparison with avertin is detailed below and will amply justify its use as the basal anæsthetic of choice.

Paraldehyde

Avertin

Cheap	More costly.
Stable	Not so stable.
Larger in quantity and requires care and preparation to make the patient retain it.	Small in quantity and easily retained.
Sleep comes in half an hour or more and is light.	Sleep is early and deep.
Very little muscular relaxation.	Helps materially to muscular relaxation.
Quantity of additional anæsthetic required is larger.	Quantity of additional anæsthetic required is very small.

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ETHYL CHLORIDE FOR SHORT ANÆSTHESIA

By A. GREVILLE YOUNG, L.R.C.P., L.R.C.S. (Edin.),
D.T.M. (Cal.)

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It appears that in many of the smaller hospitals in India full chloroform anæsthesia is given for minor operations. This is not necessary and I would like to suggest that the following method be tried more frequently.

Open ethyl chloride

Ethyl chloride, of course, is given easily and efficiently by means of an inhaler, but many hospitals do not possess such an inhaler. Thus we have come to use ethyl chloride on an open mask. For teeth extractions a gag is first inserted. Then a Schimmelbusch's mask with four layers of gauze is applied to the face. Round the mask a towel is wrapped in such a way as to leave only a small portion of the gauze visible as is done when giving ether. Ethyl chloride is sprayed for a few seconds on the gauze and the patient is asked to breathe deeply. The area sprayed is then covered for a few seconds by the anæsthetist's free hand or by a corner of the towel. On removing the hand more ethyl chloride is sprayed and again covered. This is repeated three or four times. If there is any cyanosis the mask is removed momentarily to allow the patient to take a breath of ordinary air. The patient is usually 'under' in one or two minutes, a fact which is easily tested by lifting one of the patient's hands; if it falls limply then the anæsthesia is complete and the operation is at once performed. By further spraying, anæsthesia may be considerably prolonged, but one is not quite sure whether this is a safe procedure. It is probably better to change over to ether or chloroform. Since trying this during the last eight months on some hundred cases we have not observed

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Often fails in alcoholics and in those addicted to drugs, making them boisterous and talkative.	Sure in action.
Requires no preliminary narcotic.	Requires a preliminary narcotic.
No contra-indications	Contra-indicated in cardiovascular and hepatic disorders.
While coming round the patient is sometimes boisterous requiring morphia.	While coming round the patient is quiet.

In conclusion I must thank Lieut.-Colonel W. L. Harnett, Professor of Surgery and First Surgeon, Medical College Hospitals, Calcutta, for kindly affording all facilities, and for help and guidance in carrying them out on the cases in his clinic.

any untoward symptoms. Occasionally we have had difficulty in getting big men, or heavy drinkers under properly and in these cases we have changed over to chloroform. It is to be noted that the anaesthesia in such cases has been quicker than with chloroform alone. Incidentally, it may be mentioned here that the mixture used by us with great success is chloroform 9 parts, and alcohol 1 part. The advantage of these short anaesthetics is that no

preparation is required. The patient rarely vomits and is able to walk home a few minutes after the operation. It saves considerable time too if there is only one operating table available. Ethyl chloride is obtainable almost anywhere. We have found the cheap variety (Schering), about Re. 1-2 for 100 grammes, quite efficient. Each tube lasts for five or even six patients, and so the cost per head is less than 4 annas.

Medical News

CONFERENCE OF THE INTERNATIONAL UNION AGAINST TUBERCULOSIS

THE annual meeting of the Council of the International Union against Tuberculosis, whose Chairman is Professor Nolen (Netherlands), was held in Paris, on Saturday, 22nd July; delegates from fourteen countries attended this meeting. At 10 A.M. an administrative session took place at the headquarters of the Union, 66 Boulevard St. Michel, Paris. It was decided that the Conference of the International Union would be held in Warsaw on the 4th, 5th and 6th September, 1934, and that the three following subjects, selected from a list of questions submitted by the various countries belonging to the Union, would be entered on the agenda:

Biological subject: *Biological variations of the tubercle virus*, opening report by Professor Karwacki (Poland);

Clinical subject: *The various forms of osteo-articular tuberculosis and their treatment*, opening report by Professor Putti (Italy);

Social subject: *The utilization of dispensaries for the treatment of tuberculous patients*, opening report by Professor Leon Bernard (France).

Mr. John A. Kingsbury of the United States will give a lecture on 'Methods in further control of tuberculosis—Report upon an experiment in a rural area characterized by a low tuberculosis rate'. According to the plan followed at Oslo and at The Hague, ten speakers selected from different countries will be designated to open the discussion on each of the three main subjects.

The scientific session which took place at 3 P.M. was devoted to a report by Dr. Saenz on 'Tuberculosis bacillæmia'. The report was followed by a discussion in which Professor Leon Bernard, Secretary General of the Union, Professor Valtis (Greece), Professor Bezancon (Paris), Professor Yevrem Nedelkovitch (Yugoslavia) and others took part.

BATH

THE following news item has been received from Bath:—

A good many prominent Indians have visited Bath, the historic English health resort, this summer. Sir Prabhashanker D. Pattani when in England never fails to take a course of the Bath waters; an Indian doctor from Lucknow recently spent a short time at Bath studying the medical aspects of the Bath treatment for rheumatic diseases and the other conditions treated by the hot springs, and now Sir Hari Singh Gour is taking the cure.

MEDICAL AND SANITARY REPORTS FROM BRITISH COLONIES, PROTECTORATES AND DEPENDENCIES FOR THE YEAR 1931

A WEALTH of valuable information about health conditions in the individual colonies within the British

Empire may be found in the annual medical and sanitary reports issued by the various colonial Governments, but very few libraries in Great Britain or the Dominions and colonies have complete files of these publications so that the information they contain is not easy of access. Some kind of authoritative summary of these periodic medical reports has therefore long been needed and the Bureau of Hygiene and Tropical Diseases has recently taken over the responsibility of preparing such summaries and issuing them as special supplements to its *Tropical Diseases Bulletin*. So far two such annual supplements dealing with the reports for the years 1929 and 1930 have appeared. A third supplement to the *Tropical Diseases Bulletin* for October 1933 has just been published summarizing the 'Medical and Sanitary Reports from British Colonies, Protectorates and Dependencies for the Year 1931'. It contains detailed summaries written by Dr. H. Harold Scott, the Assistant Director of the Bureau, of reports from forty-nine colonies, mostly tropical or sub-tropical, and follows a general arrangement, giving for each country the year's record of vital statistics, maternity and child-welfare work, school hygiene, general sanitation, housing and town planning, etc., followed by particulars of the incidence of diseases, such as malaria, enteric fever, leprosy, yellow fever, trypanosomiasis, yaws and syphilis, and the measures taken locally to combat them. Information is also given about special health campaigns and investigations carried out in the various government laboratories or in the field into problems associated with diseases met with in the particular colony.

Thus the compilation provides a means for analysing the various factors that affect the physical well-being of European and native communities throughout the scattered colonial Empire, and records the organized efforts of the various administrations to improve the health conditions in their own localities. Its primary objective is to keep medical and research officers and administrative officers in any one region informed of work done in other parts of the Empire, but the information it contains should also prove useful for those visiting the colonies and dependencies on a pleasure trip, or those who are intending to reside and take up work there, in that they may see what are the prevalent diseases they may meet with and take precautions against, and the present state of health of the countries in which they propose to sojourn.

The supplement should be of value also to those who, though themselves living in England or other temperate climates, do business in the colonies, more particularly insurance offices, actuaries, etc. For the more ready conveyance of information of a kind likely to be required by this latter class of reader a table has been added, as was asked in a review of a previous publication of these summaries, giving in more succinct form the vital statistics and other cognate data relating to the various colonies. The supplement is published at five shillings.

ALL-INDIA MEDICAL LICENTIATES' ASSOCIATION

TWENTY-SIXTH ANNUAL CONFERENCE, BOMBAY SESSION
Christmas Week, 1933

The Secretary of the Scientific Committee appeals to all the members of the profession to send their contributions on any medical or allied subjects for the scientific section of the Conference, wherein such papers will be read and discussed under the presidency of specialists in each line.

All correspondence should please be addressed to Dr. U. A. Rao, Secretary, Scientific Committee, Reception Committee Offices, 94, Girgaum Road, Bombay 4.

The Secretary, Exhibition Committee, informs the various manufacturers and their representatives that the Eleventh Exhibition of Medical, Surgical and Sanitary goods will be held during the Conference session, under the auspices of the Association.

TENTH ALL-INDIA MEDICAL CONFERENCE, 1933

The Tenth All-India Medical Conference will be held in Bombay in Christmas Week of 1933.

Members of the medical profession are requested to attend the Conference, and to make it a success by personal attendance and reading papers of medical interest. As it is not possible to send invitations to individuals, this general invitation should be taken as a personal one.

Further information can be obtained from Dr. D. D. Sathye, General Secretary, 12, Girgaum Road, Bombay 4.

FIFTY YEARS AGO

(From the *Indian Medical Gazette*, December, 1883,
Vol. XVIII, pp. 344, 345 and 359)

THE NUDDEA FEVER

It has become a settled conviction, both in and out of the profession, that it is a disease of places, of soil; and the idea of communicability from man to man, or of portability from place to place, is not usually associated with it. The contingency of 'catching' malarious fever otherwise than by visiting or inhabiting the place where its cause, whatever that may be, abides does not enter men's minds, and the surest way of avoiding or escaping it is considered to be quitting its sphere of prevalence.

Within the last few years a new outbreak of this kind has made its appearance in the districts of Jessore and Nuddea, and caused great suffering and mortality. The Government of Bengal appointed a mixed commission composed of a medical man, a civilian, and an engineer, all officers of standing and ability, to investigate this outbreak. Their attention was specially directed to the testing, by careful observation and inquiry on the spot, of two theories which have been put forward to account for these epidemics. Both these theories attribute the intensification of the fever to obstructed drainage but they differ regarding the cause of obstruction. One view is that originally propounded by the late Rajah Degumber Mitter, an intelligent and observant Bengali zemindar. He held and endeavoured repeatedly to prove by argument and illustration that the obstruction of the drainage of the country was due to the construction of roads, embankments and railways without sufficient waterway. He adduced numerous instances which seemed to establish the truth of his contention, but his facts were all one-sided, and he failed to adduce or explain negative evidence of obstruction without fever or fever without obstruction. Moreover his theory, if true, would fail to explain the progressive character of the epidemics. The other view is to our mind more plausible and probable, namely, that the obstruction is caused by

those changes of level and natural drainage which are constantly occurring in deltas; rivers getting silted up and the water having gradually to find its way through new courses; more or less logging of soil taking place during the process of change. The conclusion arrived at by the commission is that neither one theory nor the other is adequate to account for the facts.

Dr. Lidderdale, the medical member of the commission, speculates that the ordinary fever germ acquires under certain circumstances virulent properties, and that it is capable of perpetuating its virulence by being introduced into fresh fields and pastures new through the instrumentality of man, and subsequently flourishing in a suitable and congenial nidus. The doctrine that the virulence of disease germs varies and that the variation depends on the circumstances of their development, growth, nutrition and life, has much to commend it to provisional acceptance, but it must be borne in mind that the speculation is entirely hypothetical, and will remain so until by the microscope or chemical analysis the germ has been isolated and its qualities determined.

INOCULABILITY OF LEPROSY IN ANIMALS

Dr. Otto Damsch has made a number of experiments on the inoculation of leprosy material in animals. The results seem to show positively that leprosy can be communicated to animals. Portions of leprosy tissue may remain for months in the animal body without the nuclei of the cells or the bacilli contained in them losing their power of absorbing colouring matter and becoming stained and the bacilli may not only remain intact for as much as four to seven months in the bodies of cats or rabbits, but they may actually multiply. His experiments show further that, where the bacilli penetrate, processes occur which are analogous to the leprosy processes in man, not only histologically but also in their progressive character and in their tendency to infect neighbouring tissues.

Current Topics

A Report on the Clinical Value of 'Evipan'

By THE ANÆSTHETICS COMMITTEE,
MEDICAL RESEARCH COUNCIL

(Abstracted from the *British Medical Journal*, 8th July, 1933, p. 63)

ENCOURAGING accounts of the action of yet another barbiturate anæsthetic, 'evipan', which came from German surgeons and anæsthetists, seemed to the Anæsthetics Committee to warrant a thorough clinical trial. Twenty-five thousand cases are reported from that country with one death attributed to 'evipan'. Accordingly, the offer of Bayer Products, Ltd., was gladly accepted and supplies of the new drug were put at the disposal of the Committee. Evipan sodium is the sodium salt of *n*-methyl-C-C-cyclo-hexanyl-methyl barbituric acid, and dissolved freely in water, but the solution is stable only for an hour or two.

TECHNIQUE AND DOSAGE

The evipan is supplied in powder form in ampoules to which the distilled water supplied in another ampoule is added. By aspirating and reinjecting once or twice a solution is obtained which passes easily through the ordinary hypodermic needle. This is inserted into a suitable vein of the arm with due antiseptic precautions. It is advisable to have the arm held steadily by a second person because of the twitching of muscles which often comes on early after injection has begun. The solution is run in at the rate of 1 c.cm. in fifteen seconds. Dosage is determined by the characteristics

of the patient and the results noticed. Acting on a definite scale arranged according to body-weight does not give satisfactory results. An average amount to produce unconsciousness is about 3 c.cm. A good plan, recommended by Lauber of Königsberg, who has had a big experience, is to make the patient count. When the counting ceases through sleep the amount that has been injected is noted, and the same amount is further added for a short operation, and twice as much for a long one. In elderly and feeble people, and those who have gone to sleep exceptionally quickly, only half the amount which produced sleep is added. Most patients are asleep in about one minute. There is often some twitching or jactitation, but often complete relaxation of the muscles of tongue and jaw occurs early, and care is needed to preserve a patent airway. Generally speaking, 10 c.cm. is regarded as the maximum dose. When it is desired to complete a longish operation under evipan only, the needle must be left *in situ* and a further injection made when the anæsthetic effect of the first is obviously wearing off. Used in this way as much as 20 c.cm. has been injected. There is, however, a fluctuation in the anæsthesia, and we do not see evidence of any advantage in the use of evipan for other than short operations—that is, of twenty minutes or so at the outside.

SYMPTOMS PRODUCED

A deep yawn just before the disappearance of consciousness is a common symptom. The great majority of patients fall asleep perfectly quietly. Twitching of face muscles is common, and there is sometimes jactitation of limbs. In one instance tonic contraction of many muscles and brief stoppage of respiratory movements were observed. The degree of muscular relaxation varies, but is rarely extreme or sufficient for an abdominal operation. The pupil is usually moderately dilated but active to light. In the early stages it is sometimes widely dilated. The conjunctival and, generally, the corneal reflexes have disappeared at the moment of fullest effect. Even then reflex movement at the start of operation has been seen many times. The eyelids are sometimes widely separated. The effects on blood pressure are slight. There is commonly a fall of about 20 to 30 mm. Hg., which is quickly recovered from. Respiration is often somewhat slowed, but there has been seen no serious depression except in one instance when, unknown to the anæsthetist, the patient, an elderly woman, had received a full dose of morphine and hyoscine before the evipan. The combined result was respiratory stoppage requiring, and removed by, artificial respiration and CO₂ with oxygen. It is inadvisable to give any sedative before evipan. No special preparation is needed, but it is of course desirable to have the stomach empty. Subjective symptoms as described by reliable patients are a feeling of quickly increasing lassitude which cannot be overcome and loss of consciousness in a few seconds. Experience shows, nevertheless, that it is best to wait two minutes after completing the injection before beginning to operate. The length of time of unconsciousness is usually about ten to twenty minutes after an average dose. After this time the patient can talk but is sleepy, and will drop off again if left quiet. When he finally wakes he remembers nothing after the first prick of the needle. As in the case of other anæsthetics there is considerable difference in the reaction of different persons to evipan, and the exact behaviour cannot be foretold. The patient may go to sleep with no apparent difficulty and the usual signs of anæsthesia be present, and yet there may be movement on incision, to an extent demanding a supplementary anæsthetic. On the other hand, it often happens that merely 3 c.cm. give a perfectly satisfactory, though of course only a short, anæsthesia. Our experience does not corroborate the statement of Ernst that one can reckon almost always on half an hour's good anæsthesia. We are led to believe that in Germany the surgeon is satisfied with a narcosis which is not regarded as enough by most operators in this country. Certainly the German

reports describe a more constant and sufficient anæsthesia than has been obtained here by the same dosage and technique.

CONCLUSIONS

It is obvious from what has been stated that evipan is not to be regarded as a basal narcotic in the sense that, for example, nembutal and avertin are. Its action is so evanescent that it cannot be employed, as are these drugs, for procuring a longish period of quiet or of unconsciousness before the administration of the anæsthetic proper, nor can it be used, as are the basal narcotics, to put the patient to sleep in his bed in order to avoid all knowledge of transference to the operating theatre. If it is used before another anæsthetic this must follow closely on the administration of the evipan, and as a preliminary, therefore, it is to be classed with nitrous oxide and ethyl chloride rather than with the basal narcotics. For those who like intravenous methods it is certainly an admirable means of inducing anæsthesia, all opinion agreeing as to the rapidity and pleasantness with which the patient becomes unconscious. Excitement or restlessness during induction have been seen only in unusually emotional subjects. After-effects also are of rare occurrence. It can be relied on for an excellent anæsthesia in minor surgery—that is, for short operations when the possibility of slight reflex movement is not a matter of great concern. It is true that often the anæsthesia is profound, and that by repeating the injection it can be prolonged; but it is not obvious that this is a better procedure than usual methods, such as gas and oxygen, for example. The recovery free from after-effects and the quiet induction make evipan a valuable agent in the case of persons gravely ill, for whom a short anæsthesia is desired for any reason. There are many such instances, when it would probably be preferable even to nitrous oxide. Two examples of this kind may be quoted from our series.

A man, aged 62, suffering from aortic regurgitation and arteriosclerosis, had amputation of the great toe for gangrene. He received 6 c.cm. evipan. Sleep was induced in half a minute. The operation took ten minutes, during which time the anæsthesia was all that could be desired: After twenty minutes he woke up yawning and was talking a minute later. Half an hour later he fell asleep and slept for six hours.

The other example was a man of 36 years, extremely ill with empyema after pneumonia. He was regarded as unfit for a general anæsthetic. Nevertheless, it was decided to use evipan, of which 10 c.cm. were injected. Anæsthesia was good, and the operation, rib-resection, was completed without anxiety. The patient was fully awake after three-quarters of an hour, and suffered no after-effects.

A few trials have been made of the efficacy of evipan by the mouth. It is described as proving less efficient thus given, than nembutal in the same circumstances. Nevertheless, two or three of the tablets in which it is provided for oral administration are a useful hypnotic, generally causing sleep in a short space of time. It is a useful agent with which to break a habit of sleeplessness.

Cystitis and Bladder Antiseptics

By JOHN MABERLY, L.R.C.P. (Lond.), M.R.C.S. (Eng.)

(From the *Medical Press and Circular*, New Series, Vol. CXXXVI, No. 4919, 16th August, 1933, p. 151)

In the bulk of cases of cystitis some bacterial infection is present. Leaving out bilharzia, which is treated specifically by tartar emetic, two groups of organisms are found in the urine. Firstly, the Gram-positive pyogenic organisms, staphylococci and streptococci, which are found almost exclusively in alkaline urine, and are capable, especially the staphylococci, of breaking up urea and giving rise to ammoniacal urine; and, secondly, *B. coli* or, more rarely, gonococci, typhoid, or tubercle bacilli, all of which prefer, and are usually

found in, acid urine. The subject of cystitis and infected urines naturally falls into two divisions, and is most conveniently discussed under the headings of (1) alkaline urines; and (2) acid urines.

(1) ALKALINE URINES

The cause of cystitis with an alkaline urine is some factor producing lowered resistance, such as chill, injury, calculus, enlarged prostate, stricture, residual urine, followed by infection with staphylococci or streptococci, introduced from some focus within the system, or from without via the urethra, in catheterization, for instance. The chief symptoms are frequent micturition, pain about the region of the bladder, urine cloudy with mucus, and usually pus, ammoniacal or offensive to the smell and alkaline in reaction. For practical purposes the presence of Gram-positive pyogenic bacteria may be inferred from the character of the urine.

Treatment.—Normal urine being acid in reaction, our endeavours must be directed towards reducing the urine to that condition, and if by medical means we can accomplish this, we shall at the same time cure the bacterial infection, seeing that the bacteria involved can only flourish in an alkaline medium.

Several drugs have from time to time been introduced to the medical profession as bladder antiseptics. Boracic acid is, I submit, the most reliable drug in cystitis with alkaline urine, and staphylococci or streptococci infection. It is also a healing drug in the simpler forms of cystitis. The first reference to its oral administration in English medical literature appears to be a letter by Dr. G. V. Percy, medical officer to the French Hospital in London, in *The Lancet* of 19th July, 1884. The following extract will convey the purport of that communication: 'The patient on whom I first tried it was suffering from a bad stricture of the urethra and perineal abscess. His urine on admission was strongly ammoniacal with flakes of mucus. Boracic acid was administered in 10-grain doses every three hours a few days after admission. In about twenty-four hours the urine changed in reaction, and when passing through the fistula—recently formed—did not scald nearly so much. Although the boracic acid was continued for a fortnight, no harm resulted from its continuous administration. The urine passed was kept in a vessel for several days without its undergoing decomposition; it also kept its acid reaction'. The second case was 'an old woman who had suffered from cystitis of doubtful origin for seven months previous to her admission. Urine was passed every quarter of an hour day and night when she came in. There was much irritation of the thighs, and much scalding on micturition. After trying several remedies with slight success, and the urine being distinctly alkaline and fetid, the boracic acid in 10-grain doses twice a day was ordered. As in the previous case, the reaction of the urine changed after the first day of taking the mixture, and has continued acid since. Her symptoms were greatly relieved'. In both cases an alkaline, ammoniacal and septic type of urine was converted in a few hours into an acid one by the administration of boracic acid.

Some unfavourable results reported in the medical journals as having followed excessive and poisonous doses of the drug appear to have alarmed the profession, and stood in the way of its general adoption as a urinary and bladder antiseptic. Scattered through medical literature, however, we find occasional references to the use of boracic acid in diseased conditions of the urine and bladder. For instance, in Freyer's work on stricture of the urethra and hypertrophy of the prostate (1902), in discussing the treatment of cystitis with enlarged prostate, he says: 'When the urine has a tendency to become cloudy and gives off a fishy, offensive odour, the best drug to administer is boracic acid'. In most textbooks, however, the use of the drug as a bladder and urinary antiseptic, when given by the mouth, is not mentioned. For some obscure reason hexamin (urotropin) in conjunction with acid sodium phosphate has come into general vogue among

British practitioners, and has entirely superseded the older drug.

The laboratory experiments carried out on behalf of the Science Committee of the British Medical Association by Dr. Anson Jordan on urinary antiseptics (*B. M. J.*, 13th September, 1913), although they do not entirely coincide with clinical experience, throw a useful light on the subject. The most important conclusions arrived at were: First, that the antiseptic power of urotropin is entirely dependent on its disintegration and the formation of formaldehyde. Second, in neutral solutions this disintegration takes place only to a very small and practically negligible amount, and in alkaline solution not at all. Third, in acid solutions the percentage of urotropin which breaks up increases considerably in a degree related to the acidity.

The object therefore in giving urotropin as a urinary antiseptic is to exhibit formaldehyde, and this action is entirely dependent on the question whether in clinical work it is possible to raise the acidity of the urine sufficiently to have any definite effect in breaking up the urotropin and setting free sufficient formaldehyde in the bladder to be of any practical use as an antiseptic.

In test-tube experiments this can be easily accomplished by increasing the amount of acid sodium phosphate to the necessary amount, and the fact demonstrated that the drug is then a powerful germicidal agent to all types of organisms. In clinical records, however, we look in vain for any such satisfactory results, although the two drugs have been given extensively with that object. We have most of us met cases of septic or *B. coli* infections of the urinary organs in which, in spite of heavy dosing, the combined drugs have completely failed to bring about any curative result, and it is now generally admitted that clinical results negative any assumption that urotropin is dissociated in the bladder with the formation in any appreciable amount of formaldehyde, and consequently the drug may be written down as therapeutically inert. Any apparent success obtained by its administration in septic conditions of alkaline urine may with sound reason be ascribed to the acid sodium phosphate with which it has been combined.

Jordan demonstrated by means of test-tube experiments that boracic acid in the presence of urine proved inhibitory to the growth of all types of organisms. Unfortunately, however, this laboratory finding does not accord with clinical experience. In actual practice, given by the mouth, boracic acid has proved to have little or no effect on the *B. coli* or on tuberculous infections. It illustrates the necessity of checking all laboratory findings by actual clinical experiment.

My attention was first drawn to the use of boracic acid in bladder conditions in 1892. The case was that of a miner on the Johannesburg goldfields, who was suffering from paralysis of the lower half of the body, including the bladder, the result of an injury to the lumbar region of the spine. Catheterization was necessary, and the urine became very septic and ammoniacal. On the recommendation of Dr. Durr, of Johannesburg, I tried 10-grain doses of boracic acid given by the mouth twice a day. The urine completely cleared in three days, and after that a dose taken occasionally was found sufficient to keep the urine sweet, in spite of the catheterization being carried out by unskilled attendants.

Since this case I have had many opportunities of testing the value of the drug in cystitis and in unhealthy or septic conditions of the bladder associated with calculi, in residual urine in enlargement of the prostate, and as a means of preventing the occurrence of cystitis during the treatment of strictures and in operations on the bladder, such as removal of the prostate or calculi. In all these uses the drug has been found uniformly reliable when given by the mouth; apparently owing to its power of ensuring an acid reaction of the urine. It fails, however, to show any definite therapeutic action in acid urine with *B. coli* present.

The following are some examples of the use of boracic acid:

Case 1.—A man, eighty-three years of age, had for some time found increasing difficulty in passing urine, and the last month had been catheterized daily. In spite of taking acid sodium phosphate and urotropin, his urine remained turbid, alkaline, and unpleasant in odour. His medicine was changed to ten grains boracic acid with five minims of nux vomica three times a day. At the end of three days the urine was acid and clear.

Case 2.—A man, aged seventy-six, had been operated on for enlarged prostate, and was suffering from permanent incontinence of urine, for which he wore a rubber apparatus. His urine was alkaline and septic. He was given five grains of boracic acid with tincture nux vomica three times a day. Three days later his urine was acid and sweet.

Case 3.—A man, aged sixty-four, who was being prepared for a removal of the prostate. He had been on a mixture of acid sodium phosphate and urotropin for some time, but continued to pass a good deal of mucus and pus in the urine. He was changed over to five grains boracic acid and five minims of tincture nux vomica. The urine completely cleared in a week. He made a rapid and uninterrupted recovery from his operation. An occasional dose was given as a prophylactic after operation.

In cases of old men with enlarged prostate who are unsuitable for operation and have to depend on catheterization, and in those cases with a limited amount of obstruction who can manage without catheterization and refuse operation, the administration of boracic acid ensures an acid urine, and the absence of pyogenic organisms. There is neither necessity nor is it wise to keep these cases continuously dosed with the drug, but merely to keep a supply of their medicine handy, and take a dose or so when necessary. I have found it a convenient plan to supply them with a little blue litmus paper, and advise them whenever the urine failed to turn it red, to take a dose or two of their mixture. I believe that if this method of treating the bladder were generally adopted in prostatic cases prior to and after operation, the results would be more satisfactory, and a large number of cases, which under the usual methods of medication are considered unsuitable, could with advantage be submitted to operation.

Boracic acid, when taken by the mouth, not merely renders the urine acid and unsuitable for the Gram-positive bacteria, but also has a healing action on the mucous membrane of the bladder, although no septic infection is present. In the case of a man with a calculus lodged in the prostate, for instance, the administration of the drug not only did away with the irritable condition of the bladder and frequent micturition, but reduced the amount of pus, which microscopically was sterile, from about one-third in the urine glass to a very small fraction within ten days. In simple cystitis the drug cuts short the attack remarkably rapidly. Boracic, or boric, acid (H_2BO_3) was originally suggested by Pasteur, in 1864, as a possibly useful drug in ammoniacal urine, on the grounds of its then recently discovered preservative and anti-fermentation action in putrescible organic fluids such as milk, etc., and not for any bactericidal action. The rôle of the microbe had not then been discovered. It is a weak acid, and, as such, less germicidal than the majority of the mineral acids. In weak solutions it inhibits the growth of some bacteria, but even saturated solutions do not kill pathogenic germs. Certain fungi are, however, killed by very dilute solutions.

When taken by the mouth it is eliminated chiefly in the urine. Although excretion begins within fifteen minutes, and may be quite rapid at first, so that 50 per cent of the ingested quantity will be passed in twelve hours; the balance is excreted more slowly. Thus the drug may be detected in the urine three to five days after the last dose has been taken.

It would appear that the anti-bacterial action of the drug, when given by the mouth, is not due to a true

germicidal action, but rather to its power of rapidly converting alkaline into an acid urine which is no longer suitable for the growth of the Gram-positive pyogenic organisms. Like most active drugs, when given in excessive doses it exhibits poisonous properties, chiefly disturbances of the digestive organs, such as vomiting or diarrhoea and nervous prostration. In doses of five to ten grains, taken two or three times a day, the possibility of any poisonous symptoms appearing may be ignored, especially as it is rarely necessary to continue the administration regularly over a long period. In order, however, to be on the safe side, especially in debilitated subjects, I usually add two to five minims of tincture nux vomica to each dose, and although I have given the drug in a large number of cases, I have never seen any ill effects.

A convenient prescription is the following:

R̄ Aëidi borici	..	60 grains
Tincturae nucis vomicae	..	30 minims
Aquam ad	..	6 fluid ounces
Fiat mist.		

One or two tablespoonfuls to be taken three times a day if necessary. Oral administration is more effective than bladder irrigation in surgical cases.

(2) ACID TYPES OF INFECTED URINE

The colon bacillus is now recognized as far and away the commonest cause of pyelitis, cystitis, and ulceration of the bladder associated usually with acid urine. Cholecystitis and nephritis are not infrequent complications. The colon bacillus is a normal inhabitant of the intestines, and apparently reaches the urinary organs by the urethra or through the lymphatic vessels. Colon bacilli infections are of two types.

(a) *Acute*: in which there are signs of a general toxæmia with constitutional reaction, and usually an intermittent temperature. (b) *Sub-acute or chronic*: in which *B. coli* are found in the urine, without any marked constitutional disturbance, but usually with some symptoms, such as pain in the region of the kidneys, increased urination, and a cloudy, acid urine.

Probably *B. coli* infections of this type are more frequent than is generally suspected, especially among women. The chronic forms may be the sequelæ of acute attacks, in which case the urine is likely to contain a definite amount of albumin.

The diagnosis of colon bacillus infections is in many cases, from merely clinical evidence, a difficult matter. The assistance of the microscope is necessary in order to arrive at a positive conclusion.

(a) The acute forms of colon bacillus infection are sudden in onset, although they may be preceded by those of a sub-acute type, such as pain in the kidneys. Two symptoms are commonly present, namely, an intermittent or remittent temperature, and in many cases nausea or vomiting. The temperature is characteristic, usually intermittent, rising in the afternoon or evening to 100° or 103°F., and returning to normal or sub-normal in the morning. The intermittency or remittency of temperature reminds one of the remittent fever of the allied typhoid infection, the exacerbations taking place at a similar time of the day. Nausea and vomiting may be absent, but in some cases vomiting is very severe and persistent, and is inclined to mislead one as to the true nature of the case. *B. coli* will usually be found to be present in the vomit. The other symptoms vary somewhat according to the organ specially attacked. With cholecystitis, jaundice, pain and tenderness on pressure over the gall-bladder will be present. In pyelitis and nephritis the urine will contain albumin and possibly blood in varying amount, in which case it may be alkaline in reaction. Microscopic and cultivation tests will demonstrate the presence of *B. coli*.

(b) In the diagnosis of sub-acute and chronic forms, the failure of simple lines of treatment, such as the administration of small doses of boracic acid to clear the urine and do away with any symptoms of irritation in connection with the functions of the bladder, should

make one suspect the presence of *B. coli*, and indicates the desirability of a bacteriological examination of the urine.

Treatment.—It is generally admitted that the treatment of colon bacillus infections is unsatisfactory; alkalies, urotropin, vaccines, etc., have all proved largely failures. Personally, I have met failures with all these methods. The administration of boracic acid has also failed to have any effect. One drug, however, namely, monsonia, a South African plant belonging to the geranium family, has given most definite and curative results in the acute type of case, cutting short the vomiting and rise of temperature and rapidly reducing the number of colon bacilli found in the urine. It fails, however, in the chronic or non-feverish type of case. The first case which suggested the value of monsonia in acute colon bacillus infection was one which occurred in 1922, of which the following is a short record.

Case 1.—A woman, aged forty-six, had been suffering for some time from indefinite malaise and pain in the right lumbar region. When I first saw her she was dangerously ill. Severe rigors occurred daily about 4 P.M., with a rise of temperature to 103°F. Headache, nausea, and vomiting; pulse rapid and irregular; pain and tenderness on palpation of the right kidney. The symptoms eased towards mid-night, and the morning temperature was normal, or very slightly above. The urine contained a trace of albumin, the centrifuged deposit showed moderate number of pus and epithelium cells, and numerous coliform bacilli. The symptoms recurred for three days under the methods at first adopted. The gastric disturbance grew worse, and severe vomiting occurred. The vomit showed bacillus coli on culture. With the idea of counteracting the gastric symptoms I ordered the following:

R. Tincturae monsoniae	.. 25 minims
Acidi hydrochloridi dil.	.. 2 minims
Aquam ad	.. ½ ounce

to be taken every eight hours.

The result was that not only did the vomiting cease entirely after the second dose, but the other symptoms showed a marked remission. The third day the temperature remained normal. The centrifuged deposit of urine showed a remarkable decrease in the number of coliform bacilli, so much so that the bacteriologist suggested that those present were possibly contaminations from the external parts. Unfortunately I was not able to follow up the case as I was only temporarily in charge, and handed the patient back to the regular attendant on the fourth day. It had, however, demonstrated the probability of monsonia having a definite action in colon-bacillus infections. The fact that the drug had already proved antagonistic and raised the resistance to *B. typhosus* and the paratyphoid organisms, made it appear that it was not improbable that it would have a similar action on colon bacilli. Since this case a series of interesting results in various types of acute colon-bacillus infections have been obtained, which strongly support this view, and indicate that in monsonia we have a valuable drug for the curative treatment of these cases. The following is a résumé of the evidence:

Case 2. Ulcer of bladder.—A girl, aged twelve years, had been suffering for three years from recurrent attacks of hæmaturia, with painful micturition and an intermittent temperature. *B. coli* were plentiful in the urine, apparently it was a case of ulceration of the bladder. I unsuccessfully treated her at Capetown for one of these attacks prior to my discovering the value of monsonia. She went to England and underwent a three months' course of hospital treatment, including a series of vaccine injections. On returning to Capetown all the symptoms recurred, and I gave her the following mixture:

R. Tincturae monsoniae	.. 15 minims
Acidi borici	.. 5 grains
Aquam ad	.. ½ ounce t.d.s.
ter in die.	

She took this for ten days, and the urine then gave a negative result as regards *B. coli*. She remained free of any recurrence for the next two years, during which she was under observation.

Case 3.—Woman, aged forty, 7th November, 1923. She complained of pain on micturition, with frequent desire to pass urine, for the last three weeks. During the last few days she had suffered from sharp shivering attacks, and rise of temperature with a feeling of faintness in the afternoon. Examination by bladder sound gave a negative result as regards possible stone. Bacteriological examination showed the presence of *B. coli*. Tincture of monsonia, 20 minims, boracic acid, grains five in water, to half an ounce, was prescribed three times a day. By 11th November all symptoms had disappeared, and the patient was normal. She continued taking her medicine for a week, and had remained in sound health for twelve months, when last heard of. A second bacteriological test of the urine was not made.

Case 4. Acute infection very similar in character to Case 1, with heavy deposit of albumin in urine.—Mrs. G., aged sixty, had been complaining for three months of pain in the region of the left kidney. 10th January: was suddenly seized with an attack of vomiting. On arrival at 10 P.M. I found the patient in a collapsed condition with a rapid, irregular pulse, temperature 101.2°F. She had been vomiting bile-stained fluid since 3 P.M., and could not retain even water. I gave her a hypodermic of morphia, gr. ¼, hyoscyne hydrobrom., gr. 1/200, and digitalin, gr. 1/100. She had a quiet night. The next morning I put her on a similar mixture of monsonia as Case 1. The patient steadily improved, but the temperature continued to rise in the afternoon to 99.4, and on the fourth day boracic acid, 5 grains, was substituted in the monsonia mixture for the dilute hydrochloric acid. Two days later the temperature remained normal, and continued so subsequently. The urine at first contained about one-third albumin, this rapidly decreased in quantity, and at the end of two weeks was reduced to a trace merely. After the first ten days the monsonia mixture was changed to one of 5 grains of citrate of iron and ammonia, with 5 minims of tinct. nux vomica. The patient quickly regained strength, and was able to move about at the end of three weeks. I was unable at first to obtain a bacteriological examination; the symptoms, however, left little doubt that *B. coli* were the cause of the trouble.

Case 5. Acute nephritis due to *B. coli* infection.—Girl, aged eight years. 20th May: this patient came under my charge fourteen days after an acute attack of fever, vomiting and hæmaturia. The temperature had been of an intermittent type at first; the last two days before I saw her it had remained normal or sub-normal. The urine, which was heavily charged with altered blood, showed many pus cells, and coliform bacilli in large numbers. She had been on an alkaline line of treatment and milk, which was often vomited. I changed her over to a similar mixture of monsonia and boracic acid, as case 2, and allowed a mixed liquid diet, which was retained. After three days' treatment the urine was again submitted to bacteriological examination. The report was that stained preparations of the centrifugized deposit showed scattered leucocytes and one or two Gram-negative bacilli only. The urine steadily improved in colour, and all symptoms of gastric disturbance disappeared. The urine was again examined on 1st June. It then only contained a trace of albumin; a few coliform bacilli were still present. In taking the urine, precautions were used as far as possible to avoid contamination from the external parts, but could not be guaranteed. In private practice patients object to the passage of catheters for merely scientific purposes.

Case 6. Colon bacillus infection of the gall-bladder.—The patient was a middle-aged woman who had been in bed suffering for five weeks from jaundice, occasional vomiting, pain and tenderness in the region of the

gall-bladder with persistent intermittent type of temperature. Her medical attendant, of whose practice I was temporarily in charge, had diagnosed it as cholecystitis with *B. coli* infection, and had been giving urotropin and alkalies without any effect. After trying 15-grain doses of sulphate of soda three times a day, I changed her over to tincture of monsonia, 25 minims, and dilute HCl, 5 minims, aq. ad 1 oz. t.d.s. The rise of temperature ceased after two days, and the patient was convalescent at the end of a week.

In these six consecutive cases of *acute colon bacillus* infection, five in which the kidneys or urinary bladder were apparently the primary seat of infection, and one in which the gall-bladder was affected, the effect of the administration of monsonia with either dilute hydrochloric acid or boracic acid was very definite and rapid.

(1) Vomiting and nausea ceased after one or two doses, including a case in which *B. coli* was demonstrated in the vomit.

(2) Any intermittent temperature present disappeared by the third day of treatment, except in Case 4, where it did not entirely cease until boracic acid was substituted for dilute hydrochloric acid in the mixture, probably owing to some secondary infection in the bladder, possibly one of the moulds.

(3) The actual disappearance, or very marked decrease, of *B. coli* in the urine was evident after three or more days' treatment in the cases in which it was tested.

(4) The amount of albumin present rapidly decreased, and the general condition of the kidneys improved in two cases in which heavy amounts were present prior to administration of the monsonia mixture. The preparation of monsonia which I have used in England is Martindale's tincture of monsonia.

These cases clearly demonstrate that monsonia when taken by the mouth acts as a selective internal antiseptic in acute types of *B. coli* infection in which those microbes have invaded the tissues and set up a certain amount of constitutional disturbance, as in nephritis or cholecystitis. The drug has, however, one limitation, it does not appear to necessarily prevent the propagation of the *B. coli* in the urine, or possibly at the surface of the mucous membrane of the bladder or hilum of the kidney in non-feverish cases.

In Case 5 it will be noted that although the kidney and general symptoms were rapidly relieved, and the number of colon bacilli most remarkably reduced, after three days' treatment, they were still present to a limited amount in the urine after a fortnight's treatment with the drug. The same persistence of the organisms in the urine was found in a case of a male adult, in which *B. coli* were discovered microscopically without giving rise to any definite symptoms. The patient, who was an old neurasthenic war patient, complained merely of the necessity to get up about twice during the night to urinate. The urine was slightly cloudy. The centrifuged deposit showed many Gram-negative coliform bacilli, a few leucocytes. No red cells or casts. Reaction acid. Cultures gave *B. coli*. This patient was treated with tincture monsonia and boric acid without any improvement for a fortnight. He was then given citrate of potash, 40 grains, three times daily, until the urine was distinctly alkaline, and was then again given monsonia and boric acid. There appeared to be a decrease in the number of *B. coli* present, but they failed to entirely disappear from the urine after three weeks' treatment.

The conclusion, which I think is correct, is that monsonia is ionized in the blood and tissues, and acts in them in a manner antagonistic to the colon bacilli in all feverish cases, but does not act in these microbes when they are free in the urine, or possibly infecting only the surface of the mucous membrane of the bladder when there is no constitutional reaction, such as occasional rise of temperature, to assist its action.

The formula used has varied somewhat. In acute cases it seems desirable to give full doses of tincture monsonia as long as the temperature remains remittent

or intermittent, in order to give the drug the best chance of destroying the infection during that stage, when experience proves it is best able to exert its action. Thirty to sixty minims taken every six hours with 5 minims of dilute hydrochloric acid, or 5 grains of boracic acid and water to half an ounce, is a satisfactory method.

The treatment of the chronic, non-feverish types of *B. coli* infection of the bladder and urine which many observers consider most satisfactory, is the administration of citrate of potash in 30- to 60-grain doses three times a day until the reaction of the urine is alkaline, and after that occasional doses sufficient to keep it on the alkaline side for a lengthened period.

B. typhosus infection of the urine does not appear difficult to get rid of. One case of a private soldier during the war was sent into my wards at Roberts Heights as a typhoid carrier; *B. typhosus* being present in the urine. He was treated with 5 grains boracic acid and 3 minims of tincture nux vomica, taken three times a day. At the end of a fortnight his urine was found perfectly sterile, both microscopically and culturally.

As to tubercle bacillus, we all know that drugs have so far failed to have any definite effect on that organism.

In conclusion I submit that the guiding principle in the treatment of the various types of cystitis should be the reaction of the urine. Alkaline urines, provided blood is not present, are found in simple cystitis or associated with infection by staphylococci or streptococci. Boracic acid administered orally is specific in these cases, chiefly on account of its power of rapidly converting the urine to an acid type. The treatment of cystitis with acid urine, which is commonly associated with infection by *B. coli* with or without marked constitutional disturbances, and sometimes complicated with pyelitis, nephritis or cholecystitis, is a more difficult problem. In acute forms, with intermittent or remittent temperature, monsonia acts as a curative agent. In chronic or sub-acute non-feverish types the production of an alkaline reaction in the urine by the administration of potassium citrate or one of the allied drugs appears to be the best form of treatment.

Mortality in 985 Cases of Diabetes Mellitus

By JOSEPH HAJEK, M.D.

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THROUGHOUT the United States the death rate from diabetes is increasing. In New York City this disease now causes over 1,900 deaths annually, and this despite the fact that the prevention and treatment of diabetes is well understood. The diabetes death rate in this city is about 50 per cent higher than it was only twenty years ago. Most of the deaths are in persons over fifty years of age, and among these there are twice as many victims among women as among men. Following is the record for the past ten years:

DIABETES, DEATHS AND DEATH RATE PER 100,000

Year	Deaths	Rate
1922 ..	1,448	24.4
1923 ..	1,360	22.4
1924 ..	1,177	19.0
1925 ..	1,313	20.8
1926 ..	1,485	23.0
1927 ..	1,461	22.2
1928 ..	1,663	24.8
1929 ..	1,726	25.3
1930 ..	1,784	25.6
1931 ..	1,921	27.1

Since diabetes most frequently occurs in people past middle life, this increase in mortality cannot be explained and may only partly be accounted for by the larger number of persons attaining to 34 years of age and over.

The diminution in mortality at St. Luke's Hospital is considered in this paper with reference to coma, hypoglycemia, arteriosclerosis, infection, surgery, age and sex.

Coma.—Our decrease of 7 per cent in general mortality is entirely accounted for by the 10 per cent diminution in deaths due to coma. Banting's discovery of insulin has taught us to treat diabetic coma and any diminution of mortality in diabetes at St. Luke's Hospital is due to that cause. In the preinsulin period almost all of our coma cases died, while in the post-insulin era out of 21 individual coma cases treated during the past 8 years only 0.57 per cent died. It would appear, therefore, that while our diabetics seldom now die of coma their life is, nevertheless, taken from them by an intercurrent disease, of which arteriosclerosis and infection stand as the chief offenders. It may be argued from the foregoing statement that since the discovery of insulin the life of the adult diabetic has been prolonged. However, according to our figures the average age at death in the preinsulin period was 55 years and remains the same for the postinsulin era. In the early postinsulin period, coma was for the first time in the history of the disease successfully combated. In the later postinsulin years the prevention of coma is practised with gratifying results. Already we see coma due to diabetes four times less frequently than we did in the pre-Banting period. The time is not far off when the occurrence of diabetic coma will be as infrequent as death due to coma is at present. It is much easier to prevent coma than to cure it. With the development of hospitals and clinics for diabetic patients early diagnosis and treatment are made possible. The widespread knowledge of the disease and its dietary management with or without insulin are factors contributing to the diminution and elimination of coma. The complete co-operation of the general wards of the hospital with the diabetic clinic is essential. Social Service training of the patient completes his educational cycle. Thus patients referred to the hospital from the clinic seldom show anything more than moderate ketosis.

In connection with the early diagnosis of diabetes the problem of differential diagnosis between coma due to hypoglycemia, coma due to ketosis, and coma due to other diseases comes up and should be stressed. The following illustrative case may be mentioned. A patient, who had long suffered from diabetes, was found on the street unconscious. She was brought into a hospital, where it was assumed that she was in diabetic coma. Insulin was administered. It was soon found, however, after examination of the blood that the patient was thrown into severe hypoglycemia (hypoglycemic angina?) and that her original state of unconsciousness was due to coronary thrombosis.

Hypoglycemia: We had no deaths the cause of which could be ascribed to hypoglycemia, but its effect causes much morbidity even if of short duration. I have yet to see a patient taking insulin for any length of time who sooner or later does not have an attack of hypoglycemia or of what he takes to be hypoglycemia. We educate our insulin cases and rightly so to watch for the symptoms indicative of this condition and impress upon them the proper measures to be taken to overcome it. Nevertheless, it must be difficult for the patient accurately to interpret the onset of the symptoms which at their very beginning are puzzling to say the least. If the patient is an adult whose insulin career is comparatively recent, he will immediately take steps to combat the symptoms whether his interpretation is correct or not. If the symptoms clear up, he assumes that his actions were proper. If on the other hand, in spite of precaution, the symptoms persist, his mind is assailed with doubts, and the physician's help is then required. Contrarily, if the patient is a child the first symptoms of hypoglycemia are most frequently overlooked and treatment is begun when severe reaction sets in. So that no matter how painstaking our theoretical education of the insulin patient may be, it is,

nevertheless, his own personal experience with hypoglycemia which helps him most. One or two attacks successfully treated by the patient himself give him confidence and set his mind at rest. It is during this period, according to my experience, in the career of the diabetic that severe reactions are most frequently met with. 'Familiarity breeds contempt.'

Does hypoglycemia or its repeated attacks cause any damage? The effect upon children and young adults remains problematical. In the diabetic past middle life the situation is more complicated. At this time cardiovascular and circulatory diseases are met with, and hypoglycemia may at times add sufficient shock to complicate an already serious condition. I am especially referring to cases falling into the group of coronary sclerosis and cardiac insufficiency. In this group of patients an attack of hypoglycemia may have disastrous effects upon the heart in precipitating what Dr. Joslin refers to as hypoglycemic angina. Strict prevention of this condition is indicated and attempted. The difficulties under which the patient has to labour in such circumstances are obvious. The initial symptoms are often most perplexing and the best thing the patient can do is to treat all such symptoms as hypoglycemia until proven otherwise. Such procedure, however, is followed invariably by hyperglycemia and glycosuria, and possibly ketosis, if the patient's interpretation was incorrect. In children the initial symptoms of hypoglycemia are easily overlooked and when finally discovered so that preventive measures may be taken the little patient may be in convulsions. In connection with this statement the case of little D. S. may be cited. This boy is 10 years old and has had diabetes for the past 8 years. He had several admissions to St. Luke's Hospital and was seen by Dr. Joslin in his New England Deaconess Hospital. He has had at least 8 severe attacks of hypoglycemia with convulsions and coma as well as many milder attacks; this in spite of the fact that his mother is exceptionally intelligent and in a sense a specialist in diabetes. The boy is bright, co-operative, and honest. He is a moderately severe diabetic (taking about 30 units of insulin per day), who within 24 hours may pass through the symptoms of hyperglycemia, ketosis, and hypoglycemia. Because of this he is rather difficult to manage. It is easier to treat hypoglycemia than to prevent it, which should certainly be the other way around, but the prevention of hypoglycemia must not be at the expense of insulin.

Arteriosclerosis and infection.—These two diseases continue to take a heavy toll of our diabetic patients. This field is largely unexplored and prevention remains the best insurance for these patients. Frequent periodic health surveys in addition to the proper management of diabetes is even of greater importance to the diabetic than to the non-diabetic. Much is accomplished in this direction, but nevertheless, cardiorenal disease, arteriosclerosis and infection account for 86 per cent of our diabetic mortality.

The percentages of deaths in the diabetic caused by cardiorenal disease, arteriosclerosis, and infection have almost doubled in the postinsulin period, while deaths due to coma decreased tenfold.

The diminution in general mortality at St. Luke's Hospital in the postinsulin period shows that the decrease of 7.4 per cent in our general mortality is entirely accounted for by the 10 per cent diminution in deaths due to coma.

A moderate increase in mortality is caused by arteriosclerosis, infection and malignancy during the post-insulin period. This increase may be accounted for by the great reduction in deaths due to coma, the more widespread diagnosis of diabetes, and by the increase in the number of people living during middle life.

Surgery.—Three out of every ten diabetics admitted to St. Luke's Hospital have a surgical condition necessitating an operation.

The surgical postinsulin group 1923-1930 comprises 257 cases with a mortality of 16.3 per cent a decrease

of 50 per cent as compared with the pre-Banting period.

Age.—The mortality as to age was greatest between 47-70 years.

Sex.—In 1916 Osler gave the sex ratio of male to female diabetics as 3 : 2. In 1931 Dr. Joslin states 'the proportion of males had decreased to 44 per cent in contrast to 47 per cent in 1921 and 55 per cent a decade before'. At St. Luke's Hospital the proportion of males has increased from 44 per cent in 1920 to 49 per cent during the postinsulin period up to 1931. The mortality sex ratio closely approximates the living sex ratio. The redistribution of sex is significant because it has taken place within the short space of two decades.

SUMMARY

(1) The mortality in 827 cases at St. Luke's Hospital decreased 7 per cent as compared with 50 per cent increase reported by the Board of Health, N.Y.C.

(2) The decrease is entirely accounted for by the diminution in deaths due to coma.

(3) A redistribution of the causes of death is taking place. While deaths due to coma diminished tenfold, those caused by cardiorenal disease, arteriosclerosis and infection have doubled.

(4) Surgical mortality in the diabetic at St. Luke's Hospital decreased 50 per cent.

(5) Neoplasm as a cause of death is on the increase in the diabetic individual.

(6) The average length of life of the adult diabetic has not as yet been prolonged by insulin.

The Rural Tuberculosis Problem in the South

By J. N. BAKER, M.D.

(From the *Journal of the American Medical Association*, Vol. CI, 29th July, 1933, p. 333)

Just fifty years ago, Koch discovered the tubercle bacillus. This 'find' proved epoch-making and comparable to the discovery of gun powder, the printing press, the steam engine, the cotton gin and the pneumatic tire, in that each of these has perceptibly modified man's previous mode of living. Within the brief span of a half century and because of this discovery, the world's outlook on tuberculosis has completely changed.

Tuberculosis as 'captain of the hosts of death' has been dethroned. Be the cause what may—and the contributing factors have been legion—this disease has been deposed from its high pinnacle by 'heart disease' and now sulkily sits as the seventh chief offender in this regard. From 1898 to 1908 the death rate from tuberculosis dropped one fourth; in the next decade, that is, from 1908 to 1918, it dropped one third; from 1918 to 1928 it dropped one half. Since 1918 the rate in the United States has dropped from 150 to 70.7 per hundred thousand and that of the Southern conference area from 140 to 80.4.

The reason for the higher mortality rate in the Southern conference area is, of course, the fact that 80 per cent of the Negroes in the United States are to be found in this area. It is a well known fact—the possible causes of which need not here be argued—that the Negro death rate is from two and one-half to three times that among the white population. Unquestionably, the general living conditions and the economic status of the Negro population is poor and has contributed in no small measure to the propagation of tuberculosis. Dublin states that in the fifteen-year period prior to 1926 the reduction in the tuberculosis mortality rate for Negroes was 44 per cent. This should offer encouragement as to the possibilities of improving the tuberculosis situation among Negroes, when the comparatively small amount of work that has been immediately directed to this population group is realized.

It is estimated that there are 250,000 people in the Southern conference area afflicted with tuberculosis. An analysis by McCain of figures available for cases

in adults admitted to sanatoriums in the Southern area during 1930 and 1931 indicates that, of the 9,785 studied, 11.4 per cent were minimal, 42.2 per cent were moderately advanced and 46.4 per cent far advanced. Do not these figures speak volumes? From these facts must be deduced two simple conclusions, to wit: The problem is big and the necessity for early diagnosis is paramount. The keynote of subsequent further progress in the control of tuberculosis must be 'early diagnosis', and this keynote has been clearly struck in our fifty years of experience. We stand to-day not only at the half century mark but also at a point half way up the steep incline where we may well look back over the years of battle and, profiting by the errors and failures of our predecessors, vigorously press forward to a complete solution of this problem.

The status of tuberculosis as a communicable disease is so well founded as to call for no argument on this point. Particular attention, and properly so, has been given in recent years to the relation of the family unit in the propagation of the disease. All factors that are presented in poverty, such as overcrowding, undernourishment and poor environment, of necessity play an important part in the widespread exposure and tubercularization of the population. It requires the spark, a positive sputum, to set off the conflagration, and the intimate contact of the members of a family unit is most favourable for immediate and intensive spread. While extrafamilial contact may be an important factor, the problem is reduced to the family unit with the appearance of manifest tuberculosis in one of its members.

The widespread exposure over considerable periods and consequent tubercularization of the population has been repeatedly demonstrated. Aronson, in a recent survey of the Southern states, found an average of 55 per cent reactors among Negro and white children in rural areas in which all factors are carefully controlled. The Mantoux test, a potent and standardized old tuberculin being used, has proved quite satisfactory. The application of the test on family groups has given valuable information as to the intensity of exposure and source of exposure for each family member. The value of the tuberculin test has been so well proved that it must be included in any comprehensive programme for the study and control of tuberculosis.

If, therefore, in the South, tuberculosis is a family problem, as I believe largely it is, its proper solution and control must revolve about the family physician as the pivotal point in such control. Until recent years the private practitioner has had a most difficult and unpleasant task in the handling of this disease in its many phases. The discouragingly low economic status of the population groups in which most of his cases have occurred has been a tremendous handicap. The physician has been forced to depend on his own ability to diagnose and treat these cases without the facilities for confirmation or assistance with roentgen examination or expert consultation. State and municipal laboratories have been of considerable aid in sputum analysis; but when the records of these laboratories show an average of 20 per cent positive of specimens submitted, this would seem to indicate that this procedure has not been fully or intelligently applied.

The experience of Southern physicians shows that many cases are seen by them but a short time prior to death. This is particularly true in the case of the Negro. With this experience, coupled with the low economic status of the average patient and feeling that death is the usual and immediate outcome, the physician naturally does not wax enthusiastic over either diagnosis or treatment. Such cases cannot bring prestige even though all may have been done that is humanly possible in a short period of time. In the absence of proper institutional facilities, where surgical procedures might be used in selected cases and where cases are too far advanced for rest to be a possible factor in recovery, a physician may do very little in the way of medical skill, except to relieve final suffering.

Organized effort, therefore, which appreciates and strives to overcome the difficulties experienced by the key man—the family physician—seems to offer much hope for success. Teamwork of the finest sort and a sympathetic understanding should exist between each physician of the organized medical profession and the official county or municipal health department. The extent and complexity of the local problem must be presented to both the medical profession and the lay organizations. A study and summary should be made from existing records and presented in acceptable form to each group. It is only in this manner that a broad programme acceptable to both physicians and lay groups may be prepared and executed which will have the whole-hearted and financial backing of all concerned. The official health organization should sponsor and lead in the education of the people and in the publicity and organization necessary to promote the effort. The methods of control advanced and stressed should be early diagnosis and treatment, isolation of all open cases, social investigation and adjustment of unfavourable environment, and intensive education of the public, especially those closely associated with the disease.

PROGRAMME BASED ON LOCAL RESPONSIBILITY

A reasonable programme which might be adopted for joint effort on the part of the physicians and the health organization should be laid down along the following lines:

(1) A programme of education, participated in by all interested agencies, the leadership to be furnished by the organized medical profession and the recognized official health bodies. Such a programme should embrace newspaper publicity, lectures, radio talks, promotional work with families and contacts, tuberculin testing of family groups, arrangement for distribution of sputum cups, laboratory containers and pamphlets, and the institution of isolation procedures.

(2) The investigation and study of the families in all deaths on record in any given community or area. This would include tuberculin testing of all contacts and examination of selected persons or families.

(3) A complete survey of all families in which there exists a known, manifest case of tuberculosis, with the inauguration of all recommended procedures for prevention of spread.

(4) Classification of all suspects on record through local diagnostic facilities. This rather large group can thus be considerably reduced and permits of more intelligent effort where needed.

(5) The stressing of the needs for local hospital and diagnostic facilities and the provision of funds necessary for their maintenance.

(6) In the absence of proper hospital facilities, as is the case in many of the rural sections of the South, treatment of domiciliary tuberculous cases by the local medical profession, with the recognized agencies giving all possible aid in the matter of nursing and control services. This broad plan of co-operative effort is proving helpful in many sections in Alabama and is worthy of more extended trial.

These views, briefly and imperfectly expressed, spring from the concept of local responsibility on the part of each community, be it a township, county or what not, in regard to its own tuberculosis problem, as much so as the building of its almshouses, its jails, its schools or its roads. Spurred on by the insistent urge of its populace, many states have seen fit to take over, almost *in toto*, all their tuberculosis problems in much the same fashion as they have assumed the insane and eleemosynary burden. This is a financial load which many states, and more particularly in the South, in their present impoverished plight, will certainly experience difficulty in shouldering. When one considers the slow turnover in such institutions and the comparatively small percentage, usually not more than 15 or 20, of the total tuberculosis problem actually solved through this plan of state co-operation, one can but wonder whether this is either the sounder or the more economic

channel of approach. No one, to-day, would question an important degree of responsibility on the part of the state; the question is rather how best this responsibility may be discharged. To assume the entire burden, as many states have already done, is one, but an expensive, way. For a state to form a partnership with its various political subdivisions whereby it participates both financially and in the stimulation of a local programme of self aid certainly has much to commend it. The autonomy of local self government is thereby preserved and the initiative and independence of each political unit correspondingly enhanced. For these reasons, the development of the county or the district sanatorium plan, in which the state participates in both a financial and a supervisory way, seems to offer a method of approach which is sound, economically and basically, and which should form at least a beginning for those states whose finances will not justify a more pretentious programme.

To such a modest approach in hospitalization can be added a statewide programme of consultative and x-ray service such as is now being sponsored at many points. Such a scheme, as outlined, which seeks to attack the problem of control from the periphery rather than from the centre, has been planned for Alabama.

PLAN OF LOCAL CONTROL

The problem of tuberculosis control within the several states presents so many variants and is of such complexity as to defy uniformity of approach or standardization of practice. What might apply to one state in affluent circumstances and with a largely urban population would not at all apply to another with a large rural or agricultural population and with cramped financial resources. Into the latter category most of the Southern states fall. Because, also, of the fact that the county forms the political unit of government in the South to a greater extent than prevails in many Eastern states where the township dominates the political picture; organization for many types of health service has been simplified and expedited. In Alabama, for example, where up to now 80 per cent of the counties have been provided with all-time health service, it is felt that the possibilities are promising of further expanding and superimposing on an already existing county setup a simple and workable plan of local tuberculosis control. Up to the present time, so far as my knowledge goes, no one has succeeded in clearly defining the salient points that should be incorporated into such a plan, nor has there been pointed out the superfluous things that need not be so incorporated. Some two years ago and because of the many shapeless gropings in which we were floundering, Alabama's health department set for itself this rather pretentious task. A tentative plan, embracing the cardinal points enumerated, was submitted to the International Health Board of the Rockefeller Foundation and an appeal made for financial aid in its prosecution. After an exhaustive study of every detail, including the proposed field of operation and the personnel to be employed, the Foundation generously consented to make such a study financially possible. This study has been in progress now for one year.

In essence, its purposes are:

(1) To determine the incidence of all manifestations of tuberculous infection under conditions that exist in a rural community and their potential significance in relation to clinically manifest tuberculosis.

(2) To ascertain the principal channels of spread in a rural community and the factors that modify its transmission.

(3) On the basis of the information thus obtained, to devise practical preventive measures suitable to local conditions.

The general plan of procedure will be as follows:

(1) The family or household is the unit of study and all families in which there now exists, or where at some time a member has suffered with tuberculosis, will be the nucleus for the study of the disease.

(2) The search for new cases will be conducted on a countywide basis, all available means being used.

(3) A complete tuberculin survey will be undertaken to include (a) all school children, both white and coloured; (b) adults and preschool children by precincts or beats; (c) municipal and industrial groups. This should serve to indicate the difference in the incidence of infection in town and rural areas.

(4) In areas selected, on the result of tuberculin tests, an epidemiologic survey of the families within the areas will be made, with follow-up roentgen examination of selected positive reactors.

(5) The clinic is mobile and equipped with portable x-ray apparatus. Seven convenient points within the county, where electric current is accessible, have been selected as clinic centres. Provision is always made in preparation of schedules to render prompt service in all cases referred by physicians. Such physician is provided with cards and stamped envelopes to facilitate the immediate reporting of cases.

(6) A fully equipped laboratory is set up in the central clinic, located in Opelika. The value of frequent sputum examinations is emphasized to physicians and patients. A minimum series of ten negative sputums or two successive positives is the strict policy. In all positive sputum cases, bimonthly specimens must be submitted. Specimen containers are stamped, six being given on the first visit, and are submitted by the patient on a prearranged schedule.

(7) All families in which manifest tuberculosis exists are recorded individually, by family, and the observations for each family kept up to date on a family graph.

(8) General educational measures are carried on both by the clinic and by the county health staff. Each manifest case is under the care of the physician chosen by the patient, and excellent co-operation is being had through the organized local profession.

(9) When a sufficiently large group of manifest, sputum positive, tuberculosis cases have been discovered, over the age of 18 years, the preventive phase of the programme will be initiated. This will consist of a division of these families into a study and control series. The only variant in procedure with the two groups will be the initiation of isolation of cases in the study group, the portable, screened cottage, separate screened porches and separate rooms being used when possible. All patients and contacts will be re-examined and serially roentgenographed at intervals.

(10) The administration problem of rural tuberculosis control will be studied intensively in the entire county where hospital facilities are not available.

Obstetrical Errors

By E. FARQUHAR MURRAY, M.D., F.R.C.S., F.C.O.G.

(Abstracted from the *British Medical Journal*,
1st July, 1933, p. 1)

It is important that the art of obstetrics should be as highly organized as possible. If engaged for a case we must assume full responsibility and not relegate to a nurse or midwife those matters which are essentially medical and obstetrical. Again, if we are usually called in by a certain midwife and find a condition which could have been recognized, and possibly prevented, at an earlier stage, then it is our duty to educate that midwife to the value of closer co-operation. One of the biggest errors made, and still being made, by the profession is that of allowing obstetrics to drift into the hands of midwives, clinics, and whole-time officers. Some of this may be inevitable and even desirable, but doctors are losing the supervisory and consultative interest in this work to the detriment of their practices. The backbone of a successful practice is midwifery, followed by child welfare.

ANTE-NATAL CARE

The supervision, manipulations, and decisions concerned with ante-natal care form one of the most fascinating studies in medical art. The absence of this

care is a big error. The multitude of normal labours which occur without such supervision tend to belittle its value and to make people somewhat sceptical. Sooner or later a most devastating tragedy will shock the most casual in this regard. Such comparatively simple and not infrequent matters as the recognition of an occipito-posterior, a breech in a primipara, or a contracted pelvis which invites obstruction may, when properly dealt with, make all the difference between a triumphant success and maternal and foetal exhaustion, bruising, and even death. Ante-natal care is not merely safeguarding the lives of the mother and her child, but also making certain that they will emerge from their joint experience—the confinement—as undamaged from wear and tear as possible. What we have to aim at is that every baby is presenting head first as a polar lie and with its back anterior, and that the relation of the head to the pelvic cavity shows no unfavourable disproportion.

Occipito-posteriors are best dealt with by applying a pad over the child's back, and it is fixed in position with a tight binder. The bladder and bowels are kept empty, and the patient remains in bed for twenty-four hours. If the procedure fails, repeat it at the next week-end; and if it still fails, then apply it at the onset of labour.

In breech cases the error is often in diagnosis: the buttocks are mistaken for the shoulders. Palpate for the head at the fundus, and dip the fingers into the pelvis behind the pubic bones to feel for a deeply engaged head. Finally, make a vaginal examination. By one or other of these means it should be possible to arrive at a diagnosis. In cases of breech with extended legs, the lower pole of the foetus feels very like the foetal head. If faced with a breech presentation in a primipara ask yourself 'Why is it presenting as a breech?' and exclude the presence of a contracted pelvis. If the pelvis is badly contracted leave alone and arrange for a Cæsarean section, but if normal or doubtful then do a version and test the head to the brim. In carrying out a version always lubricate the abdomen with soap or oil; this makes the version easier. If failure results then try under anaesthesia. If there is still failure, then by means of external measurements and a careful estimation of the pelvic capacity per vaginam decide whether or not there is sufficient room for the breech to come through, always allowing for manipulations for possibly extended arms or legs. Failure of judgment in this respect will end in a very difficult extraction with a stillborn child, or, in gross cases, in retention of the head above the brim. Lubrication of the hands, gloved or otherwise, with ethereal soap makes the corrective manipulations during delivery much easier.

Contracted pelves are usually contracted at the brim or throughout. Some are only contracted at or towards the outlet, and they are the more treacherous, as the head engages well and gives an appearance of normality, while late in labour the moulding and caput may suggest proximity and invite a delivery with forceps. Pelvic measurements, therefore, should always be taken of the outlet as well as of the brim. With the more common types of contracted pelvis the head is high and even overriding the brim. This in a primipara is always suspicious, as the head is usually deeply engaged for some weeks before term. Measure the pelvis and test the head to the brim, if necessary under anaesthesia. With a reasonable degree of care it is possible to divide cases into those that *will*, those that *won't*, and those that *may* come through. The first are normal, the second are for Cæsarean section, and the third group should be as small as possible. Such a thing as a trial labour should not be allowed to occur outside a home or hospital, unless expert assistance is available. There is a place for induction of premature labour, but only in cases with minor degrees of contraction, occasionally in primiparae, and rarely in atypical forms of deformity.

Absence of ante-natal care may allow the toxæmia of pregnancy to produce the kidney of pregnancy and its major crisis, eclampsia. Regularity of the bowels, routine urine testing every fourteen days till the last

weeks, when it is done weekly, and, most important of all, encouraging the patient to report any unusual symptom will modify this danger. Oedema is not, as commonly believed by the laity, due to pressure, but is really a manifestation of renal deficiency. Don't hesitate to starve an albuminuric patient. Fluids are essential, and food may be withheld for a week or more with impunity. Fruit juice and stewed fruit and sugar may be given after a period and before proteins are added to the diet. In actual practice the routine testing of urine specimens would be best dealt with by the nurse if it can be so arranged.

The utmost need for ante-natal care is in the case of primiparae, as their first pregnancy and labour is a trial of their pelvic girdles and their metabolism. Multiparae must be watched carefully also. Their kidneys may be damaged, their lax uteri may allow malpresentations. Four such, with previously normal histories, arrived at a hospital with ruptured uteri. They had malpresentations which had been corrected by version. Three of them died. The malpresentations or the versions should have been dealt with earlier.

LABOUR

The dramatic obstetrics which impressed us as students, the difficult versions, embryotomies, decapitations, and so on, were largely owing to the absence of organized ante-natal care. The contrast between a timely Caesarean section in a case of badly contracted pelvis and a similar case dealt with late in labour *per vias naturales* requires no comment.

A great error during labour is to withhold chloroform. The patient's cries are unnerving the household, the atmosphere is tense, the doctor may be urged to terminate labour. Delivery may be the worst possible treatment in such a case. The patient, a primipara, may be only half-way through the first stage of a perfectly normal labour. Put her and the family to sleep by administering chloroform to the patient. Do not forget to do this when called in by a midwife to a case which you have never seen before. Quieten the household, get the history, and make a careful abdominal examination; then wash up and make a careful internal examination, and arrive at your final decision after sizing up the general condition of the mother and the child. Morphine may be given, and also bromides and chloral; but morphine should not be given if delivery is likely to take place within four hours of the injection.

Failed forceps, when analysed, are divisible into those due to errors of omission and those due to errors of commission. The former are neglect of ante-natal care, and the latter are forceful attempts to anticipate natural processes or incorrect attempts to remedy the neglect of ante-natal care. Cases admitted to hospital with the os uteri one-third or one-half dilated are merely given time to complete the natural process. The injection of pituitary extract is open to criticism. Having known of it being given to primiparae, and even primiparae with badly contracted pelves, I believe that the following is fairly sound advice: never give pituitary extract until you are fully conversant with obstetrics, and never to a primipara. Reserve its use for multiparae with a fully dilated os, and a head well engaged or low down, when it is merely a question of pushing or gently pulling the head over the perineum. Always dilute the extract and inject it gradually under anaesthesia. Another common cause of failed forceps is failure to recognize that the baby's head in an occipito-posterior case is not yet in the antero-posterior of the outlet. It is not always easy to detect, especially if there is much of a caput. It is still more difficult if the patient is lying in the left lateral position. Great help is obtained by delivering these patients in the cross-bed position, using either Clover's crutch or the obstetric straps to obtain the lithotomy position. The exact relation of the head to the outlet is then easily detected by inserting the left hand in the vagina in order to palpate it thoroughly, or even to feel for the ears. Once the

condition is recognized, rotate into the correct position and apply forceps, but if impossible to correct manually then correct with the forceps and reapply them, after correction, before extracting the head. Another error is to attempt extension of the head with the forceps before the occipital protuberance on the child's head has descended below the symphysis pubis: feel for it. In the third group of failed forceps are degrees of pelvic contraction. Gross cases are obvious by abdominal examination alone. Moderate cases require a careful examination under anaesthesia of the pelvic girdle and fetal head. Ask yourself what has already been done and what remains to be done. The only possible alternative at this stage, provided the child is alive, may be a Caesarean section or, occasionally, a version. Do not be misled by the small size of the os in bad cases of contracted pelvis into imagining that the patient is still in the first stage. The os may never dilate any further owing to non-descent of the head.

It is a mistake to allow tears to occur, to fail to repair those that do occur, and to admit that they have occurred. The vexed question of tears is so bound up in the public mind with neglect that it is useful to be frank with ourselves and admit that they do arise in a very large number of primiparae. Much can be prevented, much is inevitable. The really important point is to realize when a tear is likely to be inevitable, and to anticipate it by a timely episiotomy, which should be median in position. The indication for this is a tense ostium vaginae which has produced a secondary caput on the child's head, and where, with each pain, there is blanching of the vestibule. This may, if neglected, lead to two sequels: a bursting tear of the perineum, vagina, and labia, and such laceration of the sphincter urethrae as to result in laxity and incontinence of urine later. Failure to repair tears adds to the risk of puerperal sepsis, and possibly, later, of prolapse developing. As a gynaecologist as well as an obstetrician, and knowing how uniformly well properly repaired lacerations heal, I cannot but believe that, whether the blame rests with the profession or more likely, with the midwives, there is simply no attempt to repair much vaginal trauma. One error might be excused—namely, failure to recognize that an intact perineal surface is associated with concealed lacerations. Always examine for them. Repair cannot, with rare exceptions, be accomplished by means of silkworm-gut sutures; they produce an external appearance of approximation, but they rarely manage to produce actual anatomical apposition. In order to effect this catgut should be used, either buried or superficial. Repair the vaginal tube, repair the rectal tube and sphincter when necessary, bring the levators together between them, and finally repair the skin edges. Tell your nurses not to count the stitches or to admit tears. Tell them to admit bruising; the patient and her husband will thoroughly understand, and their minds be peaceful. This is not duplicity, it is common sense. A 'tear' sounds horrible, a 'bruise' sounds reasonable. When the baby has arrived examine at once for tears. If trivial, repair at once with catgut; but if severe, then wait until the placenta has arrived and do a proper and deliberate repair in the cross-bed position.

Another error is mismanagement of the third stage. The main danger is at night when time hangs heavy and one wants to 'get it over'. We are all human; but unless an anaesthetic has been administered, then it is useful to note the time of delivery and to allow at least fifteen to twenty minutes to elapse before worrying about the placenta. Leave the uterus alone, or at most feel it from time to time. It will not let you down. If an anaesthetic has been given, then the uterus may let you down, so it is best to massage it gently and note when the placenta has left. Should it be necessary to go in for the placenta, then always give an intra-uterine douche afterwards. Failure to do this is asking for sepsis. Never allow a binder to be applied until at least one hour after delivery, and palpate the uterus from time to time.

PUERPERIUM

The first three days are probably the most important. Get the bowels open early. An enema is an adjuvant, not an essential. Opening medicine should be given in twenty-four hours' time or earlier. Always be on the look out for sepsis. Influenza, pneumonia, debility, yellow atrophy of the liver, and the breasts are often provided as an explanation for a sequence of events which are in reality due to septic processes. The headaches, shivers, malaise, and temperatures of a septic process are often attributed to influenza if it is prevalent. Chest conditions of septic origin are often manifest within three days of delivery, and to the inexpert might be believed to be of accidental origin. Rapidity of pulse, with practically no other symptom than increasing weakness, can be due to hyperacute sepsis, but may be attributed to shock or hæmorrhage. Jaundice, with only moderate pyrexia, or even in the absence of pyrexia, can be due to a hyperacute hæmolytic streptococcal infection and not to hepatic derangement. Septic temperatures and engorgement of the breasts are common on the third day. Always be on your guard about sepsis; always suspect it; and always look at the perineum and lochial discharges. Never give a vaginal douche without clear proof of vaginal sepsis. In the vast majority of cases it is merely perineal sepsis: therefore arrange for local swabbing with peroxide, 20 volumes, three times a day, followed by a jug douche of borie or weak lysol; and this is all that is needed. If there is vaginal infection apply similar treatment to the vagina. Very occasionally

the uterus is to blame, but not rarely in the first instance. The difficulty of adequate nursing in outlying areas is obvious. The fact remains that such may be essential.

Three errors remain to be dealt with, although there are many others. Lysol, or any other such substance, is quite useful as an inhibitor of bacterial activity. It does not, except in its pure state, act as a reliable antiseptic. The only reliable antiseptic is a preparation of mercuric, such as the perchloride (1 in 1,000) or the biniodide (1 in 1,000). Swabs, hands, and individuals passing from case to case can never be efficiently disinfected if they depend on lysol. With rare exceptions, never examine a patient when she comes to book you. She is nervous and self-conscious, especially if she is a primipara. Internal examinations are a rarity under modern conditions of ante-natal care. Do not tell a woman that she must never have another baby unless such an edict is based on the soundest medical, surgical, or obstetrical grounds. Such advice—in cases met with—has rarely been justified. The patient fears falling pregnant, and is panicked if she does. If such advice is given, whether justified or not, it is strangely out of place that no further advice follows. Finally, we must realize that the very essence and ethics of our existence are based upon the conservation of life itself. Therefore, safeguard the mothers with ante-natal care. Remember, when you are called in to see a case, the importance of time, sedatives, and careful decisions in labour, and always be on the look out for sepsis during the puerperium.

Reviews

THE COLON, RECTUM AND ANUS.—By Fred. W. Rankin, M.A., M.D., F.A.C.S., J. Arnold Bargen, B.S., M.D., F.A.C.P., and Louis A. Bule, B.A., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Company, 1932. Pp. 846, with 435 illustrations. Price, 50s.

THIS book is the combined work of an abdominal surgeon, a physician and a specialist in rectal diseases, and reviews the existing knowledge of the diagnosis and surgical treatment of disease of the large bowel and rectum, in the light of the accumulated clinical experience acquired in the special division of the Mayo Clinic devoted to this type of work. Those who have visited Rochester and seen the degree of efficiency attained there by the collaboration of specialists will expect a masterly presentation of the subject and they will not be disappointed. Hardly anything is omitted, but it cannot be said that the resulting volume of 800 odd pages is easy reading. Brevity is aimed at throughout, with the result that the text is crowded with references to authorities, supplemented by long bibliographies at the end of each chapter, so that the work is one for the specialist to consult and not for the student or practitioner to read.

It is difficult to summarize the main features of a work which is already so compressed. Nearly three-fourths of the book deal with the diseases of the colon and with operations, leaving little more than one-fourth for the lower rectum and anus, an allocation of space which hardly accords with the relative frequency with which these conditions are met by surgeons. The opening chapter gives a clear and beautifully illustrated account of the anatomy and physiology of the large intestine, incorporating the studies of Alvarez on the movements of the contents of the colon and the functions of the ileo-cæcal sphincter, an account of recent researches on the gastrocolic reflex and the relations between the tonus of the colon and the pyloric sphincter, most important work which has profoundly influenced current methods of radiological diagnosis. A chapter on anomalies of

development leads to a review of the subject of megacolon, of which no fewer than 76 cases have been met with at the Mayo Clinic in the last three years, 62 of them of the congenital type. Except for the relief of acute obstruction, division of the presacral and inferior mesenteric nerves is the operation of election, having the advantage over lumbar ganglionectomy that it does not interfere with the circulation in the lower limbs. Chapters on volvulus, intussusception and diverticulitis follow the usual lines. The granulomata are exhaustively described and one notes that in the Clinic syphilis is regarded as one of the rarer causes of benign rectal stricture, of the 258 cases seen in 10 years only 55 had some evidence of having had syphilis, but even in these proof that syphilis was the actual cause was unsatisfactory and it seems much more likely, as pointed out by Hayes, that gonorrhœa is the commonest cause. These cases are very common in India; syphilis, amœbiasis, ischio-rectal abscess and trauma can be excluded and by far the most probable cause would seem to be gonorrhœal infection either spreading from the vagina or direct. A noteworthy fact in this connection is that in recorded series of cases 80 per cent of the patients are women.

The next four chapters deal with ulcerative colitis, parasitic diseases, mucous colitis, sprue, pellagra, constipation and other purely medical conditions, amongst which intestinal stasis receives only two pages, with the advice that surgical procedures are not required in more than 5 per cent of cases; that Arbuthnot Lane's work is not even mentioned is eloquent of the change of view on this subject. The chapter on carcinoma of the colon is an admirable account of the subject with discussion of the symptoms of the disease as affecting the various sections of the colon, clearly set out in tabular form. For carcinoma of the rectum the operation recommended is a two-stage abdomino-perineal excision, the perineal method being reserved for cases affecting the anal canal. Many tables of mortality and recurrence rates for various procedures are given, but the types of operation and the views of different

surgeons as to operability vary so widely that results are difficult to compare. Furthermore the Mayo Clinic results are complicated by the fact that many of the cases in accordance with the 5-year survival rate of 33 per cent in 551 cases and an operative mortality of 7.7 per cent in the last 260 cases of the combined operation must be considered good for a radical procedure, but it must not be overlooked that Lockhart Mummery claims a 2 per cent mortality and 47 per cent 5-year survival rate for the perineal operation preceded by colostomy, a safer method in the hands of surgeons who only do these operations occasionally. Mummery's series is of course much smaller and not very recent. Recent results of radium treatment are exhaustively reviewed with pessimistic conclusions, but hopes are expressed for better results in the future.

The remaining chapters do not call for much comment. The dangers involved in x-ray treatment of pruritus ani are stressed and destruction of the peripheral nerves by the injection of 40 per cent alcohol is advised, and is stated to have given 80 per cent of cures. Quinine-urethane is advised for the injection of hemorrhoids and the technique is described in detail. It is surprising to find no mention of the strangulation of prolapsed hemorrhoids, a common and most dangerous complication, for treatment of which directions certainly ought to be given. Another omission is the operation practised by Mummery for prolapse of the rectum by stripping up the bowel from the sacrum, packing the cavity with gauze and allowing it to heal by granulation; the results are excellent and the operation is free from danger. The chapter on methods of examination is good but no description or figures are given of the simple and efficient types of electrically illuminated proctoscopes used in the Mayo Clinic, which differ in many respects from the usual patterns.

The chapter on operative procedures is clearly written and beautifully illustrated, sacral anaesthesia is the method used in operations on the anal region, but the procedure is too difficult and trying for the patient to be suitable in India, the method of low spinal anaesthesia used in St. Mark's Hospital is simple, safe and in the hands of the reviewer has given ideal anaesthesia, far superior to any general anaesthetic. In conclusion one need hardly add that the printing and illustrations are of the highest quality; the book is one which every surgeon should possess, it reviews all recent work with a completeness to be found in no other book on rectal diseases.

W. L. H.

ROSE AND CARLESS' MANUAL OF SURGERY FOR STUDENTS AND PRACTITIONERS.—By C. F. G. Wakeley, D.Sc. (Lond.), F.R.C.S. (Eng.), F.R.S. (Edin.), and J. B. Hunter, M.C., M.Chir. (Cantab.), F.R.C.S. (Eng.). Fourteenth Edition. London: Baillière, Tindall and Cox, 1933. Pp. viii plus 1487, with 721 figures and 24 plates (16 coloured). Price, 30s.

We welcome the fourteenth edition of this well known book which still maintains its position as the most popular surgical manual in the British Empire.

The first edition appeared in 1898 and that the fourteenth edition is available only 36 years afterwards is evidence of its popularity as well as the fact that it constantly keeps pace with the advances in surgery. The present edition, again the work of Wakeley and Hunter, is no exception to its forerunners as the recent great advances in chest and renal surgery, to mention only two subjects, have both been brought right up to date. The illustrations have also been carefully edited and we note that three hundred new ones have been added including eight new colour plates. In spite of the great advances in surgery and the necessity of constantly adding fresh matter to a book of this nature judicious whittling of subjects that have become of less importance has enabled the editors to keep it within the remarkably small compass of less than

1,500 pages. Nevertheless it would be difficult to discover any essential of surgery in one of the large systems consisting of many volumes, that is not to be found in this comparatively small book also.

This book can still be classed as the best surgical friend of the medical student and young practitioner that is available in the English language. Apart from the value of its contents the method of presentation by the publishers leaves nothing to be desired and they are to be congratulated on being able to produce such a volume for the very moderate price of thirty shillings, and a further recommendation is that the book may also be obtained in two volumes at the same price.

THE TREATMENT OF DISEASES OF THE SKIN.—

By W. Knowlesley Sibley, M.A., M.D., B.C. (Camb.), M.R.C.P. (Lond.), M.R.C.S. (Eng.). Fourth Edition. London: Edward Arnold and Co., 1933. Pp. viii plus 223, with 24 plates. Price, 10s. 6d.

This is the fourth edition of this book the first of which appeared in 1912 and the third in 1920. Additions have become necessary because in the last twenty years ultra-violet ray treatment has become much used and the methods of application have greatly improved. Many new synthetic drugs have also come into use during this period and it has been necessary to include them.

The book is essentially practical and arranged for ready reference. All the skin diseases are arranged alphabetically irrespective of their aetiology or pathology and at the end of the book there are about 150 numbered prescriptions and these are referred to by their numbers throughout the text; such a method greatly lessens the bulk of the book.

Under each heading only a bare definition of the condition named is given and this is followed by outlines of the treatment recommended. Unfortunately little attention has been paid to precise phraseology and many sentences are involved and not at all clear; it is annoying to find, in a book obviously compiled for quick reference, many sentences that one has to pause over and consider carefully before one can arrive at the real meaning implied. Directions regarding treatment are also thickly interspersed with such remarks as a certain drug '..... may be tried', '..... is recommended', '..... has been found useful', etc., but the reader is left in most instances without the benefit of the wide experience of the author being quoted. In a book which obviously is made as short as possible it is surprising to find, under the heading of that rare condition keratoderma blenorrhagica, that most of the space is allotted to a list of the drugs used in treating the acute gonorrhoea of which it is a complication. This might well have been omitted, as it is much too sketchy to be of real use. Also the ten lines devoted to yaws would hardly be sufficient to enable an inexperienced practitioner to deal successfully with this disease. These final comments indicate the reviewer's opinion of the book, which is, that it is a useful compilation of a mass of information in readily available form to those practitioners who have sufficient experience to diagnose skin diseases, but it is not likely to be of much value to those inexperienced in dermatology.

P. A. M.

RECENT PROGRESS IN MEDICINE AND SURGERY, 1919—1933.—By various authors. Edited by Sir John Collic. London: H. K. Lewis and Co., Ltd., 1933. Pp. xii plus 368, with 33 illustrations. Price, 16s.

SEVERAL books have been lately published dealing with recent advances in the various branches of the profession, but no previous attempt has been made to bring together a record of post-war progress in medicine and surgery within the compass of a single volume. Sir John Collic has undertaken the task of editing such

a book and has succeeded in producing a most creditable volume. The subjects are divided into twenty-one chapters, each written by an authority on his subject, commencing with a chapter on endocrinology by the Regius Professor of Physic at Cambridge and closing with a chapter on plastic surgery by Sir Harold Gillies. The articles are uniformly excellent and the editor has succeeded in securing balance in style, length and presentation, a task often difficult when dealing with multiple authorship.

The book is recommended to the general practitioner who wishes to bring his knowledge up to date and to the specialist who desires a summary of recent progress in subjects other than his own. Both will find the material he wants in a single volume of reasonable size and price. But, as is pointed out in a foreword by Lord Horder, it is not a book for the idle hour. It abounds with facts and the field covered is enormous. It should be studied when the brain is fresh; the trouble will be well repaid.

J. C. D.

INTRACRANIAL TUMOURS.—By Percival Bailey. London: Baillière, Tindall and Cox, 1933. Pp. xxiv plus 476. Figures 155. Price, 35s.

INTRACRANIAL TUMOURS have always been a most baffling problem to the clinicians and neurologists. The reason is not far to seek. The tumours are enclosed in a rigid bony case out of reach of the palpating finger, and, in many cases, also out of reach of all modern aids to diagnosis, like the röntgenograms and ventriculograms. Localization is almost impossible because the tumours have a tendency to give rise to symptoms from distant parts of the brain by pressure and circulatory derangements. In spite of these difficulties, it is interesting to see the advances made in this realm through the efforts primarily of the American surgeons.

The book is written by the Professor of Surgery of the University of Chicago and constitutes the demonstrations and clinics given by the author to his students. It is an admirable exposition of the difficult subject and should find a hearty welcome. Most of the illustrations are original and very instructive. Though the subject has been presented from the pathological standpoint, physiological considerations, which form the basis of the study of the nervous disorders and the keynote to the localization of functions of the brain, have not been neglected. Indeed the chief merit of the book is its brilliant exposition of the various symptom-complexes in connection with the cerebral tumours through the help of the principles of physiology. The treatment has been dealt with from the operative point of view and is very thorough both as regards the pre-operative and post-operative details. The subject of anaesthesia in intracranial surgery has also been touched upon.

The get-up is excellent though the author's anathema against glazed paper is not shared by the reviewer. The book is far too advanced to be considered suitable for the ordinary medical student, for whom it is meant by the author. The post-graduate student, however, would find in it a veritable mine of information.

R. N. C.

SOME THOUGHTS ON ASTHMA.—By A. J. D. Cameron, M.B., Ch.B. Bristol: John Wright and Sons, Ltd., 1933. Pp. 174, with 4 plates and 8 illustrations in the text. Price, 7s. 6d.

THOUGH much water has flowed under the bridge since the asthma syndrome was first recognized, the problem has remained as elusive as before. Medical research has probed into the problem from various aspects, but there has been a tendency on the part of enthusiastic workers in some of these fields to neglect due consideration of the other aspects. For some, asthma is merely a psychological problem; for others, allergy and hypersensitiveness to foreign proteins plays the most important part; there is another school

that would ascribe the condition to calcium deficiency and endocrine imbalance; and the toxic element is the primary thing with still another group of workers, who would consider all the nervous manifestations of the disease, as merely due to failure of the nervous system to co-operate successfully in getting rid of the toxin. The author of the book under review is an exponent of the toxic hypothesis, and he has supported his assertion by clinical and biochemical investigation in his clinic for a number of years. 'To his mind, the toxic theory is the only one which is built on a solid foundation, a foundation which will withstand criticism on any side'.

While refraining from making any comments on the rôle of toxicosis in the causation of asthma, it is very difficult in the present state of our knowledge of the problem to subscribe to the views of the author *in toto*. There are certainly other factors which can produce a paroxysm in the absence of an exciting toxin. The treatment recommended is certainly worthy of trial, considering the satisfactory results obtain by the author.

R. N. C.

ESSENTIALS OF MEDICAL ELECTRICITY.—By E. P. Cumberbatch, B.M. (Oxon.), D.M.R.E. (Camb.), M.R.C.P. Seventh Edition. London: Henry Kimpton, 1933. Pp. xiv plus 508, with 15 plates and 132 illustrations. Price, 10s. 6d.

THE number of editions through which this well-known book has been is sufficient proof of its popularity. It has always been noted for simplicity of language and clarity of expression. In this respect the present edition is no exception.

The present volume has been considerably enlarged. The subjects of high frequency and diathermy have been revised and treated in a more complete manner, and now extend to several chapters instead of one. The author, moreover, proposes to include these methods of treatment under the heading electrothermic methods of medicine and surgery, a sufficiently comprehensive term. The expression 'high frequency' is used as a generic term for the currents employed in the various methods described.

In the chapter on medical diathermy, a brief account of the so-called therapeutic fever and the means of producing it is included.

A new series of plates showing not only the situation of the motor point, but also the muscles which they represent, has been provided. In addition to these there are sixteen new illustrations.

The present volume, indeed, can be looked on as a detailed exposition of the subject and is sufficiently complete to take its place alongside the classical works on the subject, such as that of the late Lewis Jones and others.

WHEAT-, EGG- OR MILK-FREE DIETS WITH RECIPES AND FOOD LISTS.—By R. M. Balyeat, M.A., M.D., F.A.C.P. Assisted by E. M. Rusten, M.B., M.D., and R. Bowen, B.A., M.D. Philadelphia and London: J. B. Lippincott Company, 1933. Pp. xi plus 149. Illustrated. Obtainable from Messrs. Butterworth and Co. (India), Ltd., Calcutta. (Publishers). Price, Rs. 7-14.

THE question of human sensitiveness to certain foods as the causative factor in certain allergic diseases has been the subject of controversy for a long time. As the result of recent studies, several definite conclusions have been arrived at. One of the most important amongst them is that food sensitization is the sole cause in some cases of asthma, and a contributing factor in many, and that it is the primary causative factor in a large percentage of cases of migraine and urticaria.

In allergic diseases, as soon as the sensitization of a patient to a specific food-stuff is recognized, that particular food is usually withheld, provided it is one of the uncommon kinds. The real difficulty, however, arises when such food-stuff is a staple constituent of

diet, such as wheat, egg, and milk—which, it is recognized, are extremely difficult to eliminate from the daily dietary.

In treating a large number of such sensitive patients, the authors have realized the importance of wheat, eggs and milk as common food-offenders in allergic diseases and their main idea in writing the present volume is to help physicians and dietitians in the proper selection of food for their patients (who are sensitive to such food-stuffs) by suggesting a variety of recipes, which are wheat-free, egg-free, and milk-free. They will also, at the same time, be of great help to the patients in selecting the proper kind of dietary for themselves.

The book is divided into six parts. The first part deals with the rôle played by food in allergic diseases. Part II deals with the methods of testing adopted for food sensitization while the next part deals with the different types of patient. Part IV which constitutes about two-thirds of the book gives an exhaustive list of recipes for wheat-, egg- or milk-sensitive patients. The next two parts of the book deal with subjects of general interest, such as food requirements of the body, food-values, and height-and-weight tables.

The book is an interesting study and we feel sure that it will be of use to those for whom it is intended.

J. P. B.

FRONTIERS OF MEDICINE.—By M. Fishbein, M.D. Baltimore: The Williams and Wilkins Company, 1933. Pp. x plus 207. Price, 5s. (Agents are: Messrs. Baillière, Tindall and Cox, London.)

THIS book is one volume of a series entitled 'A century of progress'. From the list at the end of the book it is gathered that this series consists of a collection of small volumes on various technical subjects, each being written by an American authority on the subject concerned. From the style of the volume under review, which is the only one of the series that has come into our hands, it seems that these books are essentially written for the general public, with the object of giving a brief outline in simple language of scientific progress along various paths.

Frontiers of Medicine, in our opinion, achieves this object for it gives a good general bird's-eye view of this vast subject. To the critical medical reader the book will probably not appeal for it only gives the barest outlines of the numerous branches of medicine and surgery, and the critic will note certain inaccuracies. One also feels that some steps in our progress have received more than their due amount of attention in a brief general summary of this nature, and that other important discoveries have been glossed over or altogether omitted. The book will also be of much greater interest to Americans than to readers in other parts of the world.

Nevertheless it may be recommended as a book that can be read with profit by the layman as one that will give him a broad general idea of the enormous amount of endeavour that has been expended on his behalf by the medical and its allied sciences in improving his health, prospects of long life and material comfort.

THE EXAMINATION OF WATER AND WATER SUPPLIES.—By J. C. Thresh, F. J. Beale and E. V. Suckling. Fourth Edition. London: J. & A. Churchill, 1933. Pp. xvii plus 824, with 61 illustrations. Price, 42s.

THIS book has been a work not only of standard reference to sanitarians for many years, but the guide, philosopher and friend of many medical officers of health who were distant from laboratories and advice. We doubt whether any public health laboratory could do without it, and whenever any question connected with water supplies arises it is the first book that receives reference. We note with regret that the senior author has died since the last edition appeared. Dr. Thresh

was the originator of the book, and the earlier editions (and indeed the present one) contain much of his personal experience in the examination of waters and in experimental work. If we remember rightly it was his investigations mainly, that disentangled many of the puzzles of plumbo-solvency (though there are still some remaining), and pointed to the importance of the presence of small quantities of soluble silicate in natural waters as a preventive of plumbo-solvency, and to the suggestion for its addition to waters otherwise possessing this dangerous quality.

There is little need to enlarge on the qualities of the present edition. The present authors have maintained the high standard and aims of previous editions and produced a book covering very nearly every aspect of water and water supplies (except the purely hydraulic ones) and one to which the sanitarian, whether medical officer of health or sanitary engineer, may turn with the assurance that his needs will be met, and latest information and references will come readily to his hand.

As the authors state, population and the need for water supplies grow apace. In the past, large towns in England have avoided obvious polluted sources such as large rivers and have constructed large artificial lakes (e.g., Lake Vyrnwy in Wales). But more and more, such towns will be forced to make use of streams and rivers for their water supplies (London is a case in point). Hence modes and means of purifying such polluted sources become more and more important, and the more polluted the source, the higher the standard of purification demanded, and the greater the necessity and demand for more exact and precise means of purification. Thus chlorination, chloramine compounds, ozone and activated carbon are being extensively used now throughout the world for purification of municipal water supplies, and these subjects are fully noted on and the most recent ideas and work described. The aspect is closely bound up with river pollution, and, in the past, legislation in England has not been very strict on river pollution. In the future, however, greater stringency may be necessary. On the vexed question of bacteriological standards for potability, we are perhaps not very much farther forward than we were at the date of the last edition. Of methods of examination there has been a very great increase, and if we were to use every method of examination described, e.g., species differentiation, glucose + and lactose—; utilization of citrate; methyl red, methylene blue and eosin, the Voges-Proskauer reaction; special selective media for the aerogenes group, etc., we are still left with an uncertainty as to what they all mean practically, and how to incorporate such results into some intelligible standard, if this is possible. The lactose-bile-salt method has proved satisfactory to workers in England, but in America it has not found such constant favour, owing to a large proportion of false reactions brought about by Gram-positive and spore-forming bacteria. Various explanations are given for these discrepancies such as the greater pollution of the raw waters in America, the less degree of purification effected there by filtration and the fact that chlorination does not destroy spore-forming bacteria. The result has been a multiplication of methods and media in America aiming at a differentiation of faecal (human) and non-faecal organisms.

In America, the American Public Health Association has produced certain standard methods for the examination of water and sewage which have been accorded a certain amount of acceptance and which we believe are followed by many official health agencies in the U. S. A., especially the Federal, though they have received some criticisms on both sanitary and mathematical grounds. The coli-group test is the basis of the bacteriological standard. The authors of the book under review bewail the fact that no authoritative health agency in England has attempted to bring such uniformity either in methods or interpretation. English

sanitary legislation however rather abhors a standard (e.g., the Food and Drugs Adulteration Acts which contain few standards), and this attitude must naturally be reflected in the British sanitary mind. If any standard for water does exist in England, it would be that there should be no lactose fermenters in 50 c.c.m. This may be considered a high standard, but it is in line with other English standards in factors of safety, for instance in motor car construction and in building principles. If there is any standard for potability of Indian waters, we take it to be 'negative in 10 c.c.m. for lactose fermenters'. Considering the grosser pollution and even making allowance for natural purification we think the English standard to be nearer the desirable mark for India. A similar opinion we notice is gaining ground in Malayan water supplies.

We are sure that every public health worker in India will replace his old copy by this new edition.

AUTOMATIC RURAL RECONSTRUCTION. A SUGGESTION.—By J. C. Ghosh, B.Sc. (Manchester), F.C.S. Published by the author himself. P. 154, Lake Road, Calcutta. 1933. Pp. 116. Price, As. 12.

EVERYONE recognizes the disabilities of village life in India; ignorance, poverty, disease, and debt produce conditions which to the outsider would seem to make life sometimes intolerable. Still, happiness is indefinable in general terms, and perhaps there are to-day more unhappy people outside Indian villages than in them. Nevertheless, there is general agreement that the

amenities and opportunities of civilization should be made available to the villagers of India, who constitute such a large proportion of the population. The problem has received consideration from many sides and many quarters. Missionaries, sanitarians, agriculturists, economists and politicians have made plans and many have practised them with a certain amount of success. The criticism of such efforts has been that movements whose force is directed from without, which are not grafted on to the permanent agencies dealing with village life, and which depend on the virility and energy of particular individuals are bound to fail. The demand for improvement and progress must come from within the villages themselves and be part of the innate national character.

The present booklet by Mr. Ghosh is permeated with goodwill and enthusiasm. He considers that education and upbringing in social service and friendly helpfulness is not fostered sufficiently; that this, and a preparation for a scientific and industrial career, will achieve wonders even in 10 years. The argument is rather loosely put together and suffers from being presented mainly in the form of extracts from articles on special subjects. The greater part of the booklet for instance deals with the Drugs Enquiry Committee and its recommendations, only a small part of which can be relevant to the main theme. If lacking in coherency, the booklet is interesting and has a sympathetic earnestness which must appeal to those who, like Mr. Ghosh, feel that Indian village life deserves the utmost consideration and study, and that its problems lie deeply ingrained in the life and character of the nation.

Annual Reports

ABSTRACTED FROM THE RESOLUTION REVIEWING THE REPORTS ON THE WORKING OF MUNICIPALITIES IN BENGAL DURING 1931-32. GOVERNMENT OF BENGAL. (LOCAL SELF-GOVERNMENT DEPARTMENT)

Public health.—The municipal authorities almost without exception showed energy in dealing with outbreaks of cholera and smallpox. In four municipalities only were there outbreaks sufficiently serious to be described as epidemics and when sporadic cases occurred, as they did in most places, adequate measures were promptly taken, though a few municipalities wasted money on precautions, such as the burning of sulphur and coal-tar in the affected areas, which were not likely to be of practical value. It is satisfactory to note that vaccination and revaccination were carried out as a rule systematically, and that the prejudice against revaccination showed signs of diminishing. For example in Tangail and in Dacca there were for the second year in succession far more secondary than primary vaccinations and in several other places revaccinations were numerous. In Dacca and in Pirojpur, where also revaccination was popular, there was not a single case of smallpox. Against cholera the chief safeguard must always be a really adequate water supply, which is still lacking in the majority of municipalities; but chlorination and disinfection together with anti-cholera inoculation, which appears to be accepted readily, were successful in protecting the towns against the cholera epidemics reported from several districts. It is worth mentioning that at Faridpur cholera attacked only persons who did not use the water from the town water supply.

Municipalities were much less successful in dealing with malaria, which demands, for its control, not intermittent displays of energy but persistence in a definite and well-thought-out programme, giving no immediate results. From all divisions there are reports of activity in filling up tanks and cutting down jungle. But such

activities cannot possibly have any effect on malaria unless carried out systematically and over large areas, and the finances of the municipalities forbid their undertaking them on a sufficiently large scale. It is essential therefore that municipal authorities should compel property owners to collaborate by keeping their premises in a proper state. Increased powers have been given in the new Municipal Act which it is hoped will lead to an improvement in this respect, but they will not do so unless the municipal authorities use them with greater firmness than as a rule they do their present powers. Just as frequently they hesitate to incur unpopularity by insisting on the prompt payment of taxes, so too they are reported in many instances to have taken no steps to enforce the orders issued by them on owners of private lands to carry out sanitary improvements. It is possible that in this direction they may find their task made easier by the activities of anti-malarial societies which are reported to have done good work in several towns; supported by a popular movement against insanitary conditions in a definite area, the municipal authorities are in a better position to take coercive measures than when they act on the reports of their public health staff only. At Birnagar the Palli Mandali continued its anti-malarial campaign and in addition undertook measures against mosquito breeding in the Choka Bheel on the outskirts of the town; and in a few other towns anti-malarial campaigns were carried on with the assistance of the public health department. It may be noticed that reluctance to cut down expenditure on sanitation led in many places to neglect of other important activities and in particular of the upkeep of roads.

Activities against the sale of adulterated food-stuffs were very uneven. For its size, the small town of Gaibandha did most, instituting no fewer than 40 prosecutions. The total number instituted by the municipalities of the whole Presidency Division was only 20 more. Out of this total 31 were instituted in Berhampur, resulting in fines of Rs. 540. At Dacca

there were 94 prosecutions but the fines amounted only to Rs. 196. The municipalities of Dacca Division on the whole showed the most energy against the sale of adulterated food-stuffs, and among the most active of them was Nalchiti, one of the smallest. Rajshahi Division held the second place, but generally speaking little was done in the other divisions. One of the commissioners points out that in prosecutions initiated by district boards the failure of municipalities to check the sale of adulterated food-stuffs by wholesalers has been successfully pleaded as a defence by small shop-keepers in villages, who have to buy from them. This is a matter to which municipalities in general might devote more attention. The other activities of the municipalities as regards public health work during the year under review call for no special comment.

ABSTRACTED FROM THE ANNUAL CLINICAL REPORT OF THE GOVERNMENT HOSPITAL FOR WOMEN AND CHILDREN, MADRAS, FOR THE YEAR 1932

A TRIAL of nebulinal and chloral hydrate to relieve the pains of labour has been made in the case of 50 European and Anglo-Indian women. The treatment has been tried on European and Anglo-Indians in the belief that one might expect more accurate information on the results of the treatment from this class of women than from the average Indian hospital patient. The method followed was that of O'Sullivan and Craner as far as possible. The results may be summarized as follows:—

All patients sleep for varying periods after taking the drugs. Some awake with the pains, whilst others are roused, and a few do not even move with the pains. Some patients can be roused easily and could be made to talk and answer simple questions rationally, though slowly. Other patients are roused with difficulty and then drop back to sleep. A third group cannot be roused at all. Amnesia was present in about 80 per cent of the cases that had the complete course of treatment. Even in patients who received only a partial course, the pains of labour were greatly diminished, and often very little was remembered. Restlessness was noted sometimes, but was never present to a marked extent. Uterine contractions are not appreciably diminished but sometimes there is delay with the head at the outlet, owing to the absence of voluntary expulsive efforts. Forceps were applied in six cases for this reason. No other bad effect on labour has been noted, and there is no tendency to post-partum hæmorrhage.

The treatment produces, as far as we can judge, no bad effects on the cardiovascular, respiratory, urinary or alimentary systems. There are absolutely no bad effects on the child. When the treatment is combined with a little chloroform administered as the head is being born, a practically painless labour results.

Spinal anaesthesia with novocaine has been the routine anaesthetic employed by the superintendent for all except very short operations. When one has experienced the tremendous advantages of spinal anaesthesia in pelvic surgery, one would be very sorry to have to return to general anaesthesia, particularly where expert anaesthetists are not available.

ABSTRACT OF THE EIGHTEENTH ANNUAL REPORT OF ST. DUNSTAN'S

OVER 120 of the war-blinded men of St. Dunstan's are now chartered masseurs with successful practices in different parts of the Empire. Doctors have spoken with enthusiasm of the peculiar skill of blinded men in this highly specialized branch of work. Many other St. Dunstan's men are employed as telephonists. A blinded telephonist can operate a fifty-line switch-board and take down messages in Braille shorthand at

100 words a minute without turning a hair. War-blinded officers and men are also to be found undertaking directive and administrative work, and there are persons, lawyers and public men amongst them. The majority, however, are employed with their hands at such jobs as joinery, boot-repairing and basket-making.

This report makes it quite clear that although most of the two thousand war-blinded British soldiers and sailors trained at St. Dunstan's are now comfortably settled in homes of their own and living lives that approximate very closely to those of normal citizens, the work of St. Dunstan's is by no means finished—nor ever will be until the last of them is no longer living. The same organization that set them on their feet now helps by every possible means to keep them there, pledged to look after their welfare in sickness and health for the rest of their lives. Their courage and cheerfulness are almost proverbial; but it must make all the difference to them to know that St. Dunstan's is still behind them; and that behind St. Dunstan's is, as always, the sympathy and practical support of the British public, who know the debt they owe to these men, and never fail to discharge it.

ANNUAL REPORT (1932) BY THE CURATOR OF THE LABORATORY, WITH REPORT THEREON BY THE COUNCIL, ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

ANTIRABIC TREATMENT

THE superintendent has continued his examination of the statistics of antirabic treatment, collected by the Health Section of the League of Nations from the various institutes of the world in accordance with the resolution of the International Rabies Conference (Paris, 1927). A second review referring mainly to treatment during the year 1929, the results of which were described in last year's report, has been published. A third review dealing with statistics relating to 69,541 individuals, treated mainly during the year 1930, has been completed and has also been published. The conclusions arrived at are virtually the same as those deduced from the earlier figures. No evidence has been found which suggests the existence of a superiority of any one method of treatment over any other, or, more generally, there is no evidence of the existence of a superiority of treatment by live vaccines over treatment by killed vaccines. On the other hand it would appear from the figures examined that liability to post-vaccinal paralysis varies significantly according to the method of treatment employed, the liability after treatment by live vaccines being greater than the liability after treatment by killed vaccines. A number of points have emerged from the examination of the figures for the third period, and of those for the three periods combined (170,904 persons treated). For the further elucidation of these questions, larger statistics are necessary. The statistics relating to a fourth review are now being extracted.

DISEASES OF INDUSTRY

A fresh and promising line of research has this year been commenced with regard to industrial diseases. With the co-operation of Dr. J. C. Bridge, M.R.C.P.E., H. M. Senior Medical Inspector of Factories, and Dr. Thomas Ferguson, F.R.C.P.E., Inspector of Factories in Scotland, relations have been established with the Factory Department of the Home Office. Already various investigations have been initiated, in the carrying out of which the medical authorities of the Home Office are co-operating closely with the several members of the laboratory staff.

(1) In the first place, as mentioned in previous reports, Colonel Harvey is adding to his cabinet-gallery pathological specimens relating to industrial diseases. With this in view, material is being collected

by Dr. Ferguson in Scotland, and, through his colleagues in the Home Department, from England. Already some progress has been made. No such collection of microscopic specimens exists elsewhere.

(2) Colonel Harvey has also been working at the pathology of toluene poisoning, which occurs industrially amongst users of this solvent. He is now engaged in experimental work on animals upon the effects of benzene and toluene poisoning upon the blood and blood-forming organs and the nervous system. Toluene appears to be less toxic than benzene chiefly because it is less volatile.

(3) Work has also been undertaken by Dr. Kernack in the Chemical Department upon indications of nitro-benzene poisoning in samples of urine, in the hope that it might be possible to detect its presence at a stage before symptoms had developed. A method was elaborated capable of detecting one part in 500,000. In a series of specimens from workers exposed to the vapour of nitro-benzene no significant quantity was detected in any instance.

(4) Colonel Liston is also attempting to discover the cause of the skin sepsis which is prevalent amongst workers in jute factories.

Correspondence

ON THE THERAPEUTIC VALUE OF THIOSARMINE IN THE TREATMENT OF SYPHILIS

To the Editor, THE INDIAN MEDICAL GAZETTE

DEAR SIR,—I read with keen interest the article in your February number, by Lieut.-Col. A. Denham White, M.B., B.S., F.R.C.S., I.M.S., and others, on the therapeutic value of thiosarmine, and have looked through your pages since then in the hope of finding comments, from other doctors of the status of the authors of that article, regarding the accuracy of the statements made in that article. The point to which I should like to draw particular attention is the way in which a course of five grammes of thiosarmine is shown to produce slightly better results than a course of one gramme of sulfarsenol.

In the same way the authors compare a course of five grammes of thiosarmine with one of three grammes of novarsenobillon.

They claim that larger doses of sulfarsenol and novarsenobillon are not well tolerated by patients. This is not the experience of many other doctors.

I consider that these statements are misleading.

Finally, I would like to draw the attention of your readers to the fact that thiosarmine is a preparation made by one of the authors of the article in question.

Yours, etc.,

G. V. HANUMANTHA RAO, L.O., L.M.P. (Mad.),
L.C.P.S. (Bom.).

GOVERNMENT HOSPITAL,
GUNTUR,
20th October, 1933.

DANGERS OF EXHAUST FUMES

To the Editor, THE INDIAN MEDICAL GAZETTE

DEAR SIR,—After having read the notes on the dangers of exhaust fumes, in the *British Medical Journal* of 3rd December, 1932, I am tempted to write about a similar incident in this country.

In Petlad in the month of May there was a marriage procession which I attended. In the procession the bride and the bridegroom were sitting in a motor car. All the ladies that followed were just behind the car, and, as is common in processions, it moved slowly, stopping every few yards. The engine of the car was naturally kept running. The result was that after

some time ladies behind began to faint one after the other. Twelve ladies had to be removed to their homes and it was only after some considerable time that they revived.

It is very common nowadays to use motor cars in processions, but the practice should be discouraged. Either cars should be disallowed altogether or they should be kept at the tail end of the processions to avoid such mishaps.

Yours, etc.,

K. V. ACHARYA, M.B., B.S.,
Medical Officer.

CIVIL HOSPITAL,

PETLAD,

17th October, 1933.

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL C. A. SPRAWSON, C.I.E., V.H.S., Surgeon-General with the Government of Madras, is appointed to officiate as Director-General, Indian Medical Service, with effect from the 29th October, 1933, during the absence of Major-General Sir John Megaw, K.C.I.E., K.H.P., on leave.

Major-General C. W. F. Melville, K.H.P., to be Deputy Director of Medical Services, Eastern Command, Dated 2nd September, 1933.

Lieutenant-Colonel H. W. Acton, C.I.E., Professor of Pathology and Bacteriology in the School of Tropical Medicine, Calcutta, on leave, is appointed as Professor of Tropical Medicine in that institution, with effect from the 15th July, 1933.

Lieutenant-Colonel M. Das, M.C., is appointed to act as Superintendent of the Midnapore Central Jail, with effect from the 16th October, 1933.

Lieutenant-Colonel B. Gale is appointed to officiate as Civil Surgeon, Simla East, with effect from the date on which he assumes charge of his duties.

Lieutenant-Colonel S. S. Vazifdar is allowed to return to duty, with effect from the forenoon of 5th November, 1933, and is appointed as Professor of Medicine and Clinical Medicine and Therapeutics, Grant Medical College, and Physician and Superintendent, J. J. Hospital and B. J. Hospital for Children. The unexpired portion of the leave granted to Lieutenant-Colonel Vazifdar is cancelled.

Major A. H. Harty is permitted to return to duty on 23rd February, 1934, and is appointed to officiate as Civil Surgeon and Superintendent, B. J. Medical School, Poona, *vice* Lieutenant-Colonel R. H. Candy, I.M.S., proceeding on leave. The unexpired portion of Major Harty's leave is cancelled.

The services of Major M. Fazl-ud-Din, O.B.E., are placed permanently at the disposal of the Government of the Punjab, with effect from the 12th September, 1930, for employment in the Punjab Jail Department.

The services of Major R. S. Aspinall are placed at the disposal of the Chief Commissioner, Delhi, for appointment as Civil Surgeon, New Delhi, with effect from 16th October, 1933.

Captain C. L. Pasricha, a Research Worker under the Endowment Fund of the School of Tropical Medicine, Calcutta, is appointed provisionally as Professor of Pathology and Bacteriology, School of Tropical Medicine, Calcutta, with effect from the 15th July, 1933.

The services of Captain M. Taylor are placed at the disposal of the Government of Bombay, with effect from the 25th September, 1933, for appointment as Officiating Superintendent, Central Mental Hospital, Yeravda.

The probational appointments of the undermentioned officers are confirmed. The order of seniority is as now notified:—

To be Captains

R. W. H. Miller (now Major), 28th January, 1925, with seniority 9th April, 1923.
W. Aitchison, M.C. (now Major), 28th January, 1925, with seniority 20th June, 1921.
Lieutenant J. H. Crawford, 11th May, 1932, with seniority 26th December, 1930.
G. R. M. Apsey, 20th April, 1932, with seniority 22nd May, 1931.

To be Lieutenants

D. M. Fraser (now Captain), 28th January, 1925, with seniority 9th April, 1923.
J. D. Grant, 20th April, 1932, with seniority 20th April, 1931.
W. H. G. Reed, 2nd August, 1932, with seniority 2nd August, 1931.
T. E. Palmer, 2nd August, 1932, with seniority 2nd August, 1931.
W. J. Poole, 2nd August, 1932, with seniority 2nd August, 1931.
C. J. H. Brink, 25th August, 1932.

The undermentioned appointments are made:—

To be Captain (on probation)

N. J. U. Mather, 15th August, 1933, with seniority 16th September, 1931.

To be Lieutenants (on probation)

J. G. Stoneham, 1st August, 1933, with seniority 1st August, 1932.
B. F. B. Russell, 1st August, 1933 (seconded).

LEAVE

Colonel L. Cook, C.I.E., Inspector-General of Civil Hospitals, Bihar and Orissa, is granted leave for 4 months, with effect from the 24th October, 1933.

Lieutenant-Colonel V. N. Whitmore, O.B.E., Civil Surgeon, Simla West, is granted leave, with effect from the 1st November, 1933, to the 28th February, 1934. His services are placed at the disposal of the Government of the Punjab, with effect from the 1st March, 1934.

Lieutenant-Colonel R. H. Caudy, Civil Surgeon, and Superintendent, B. J. Medical School, Poona, is granted leave for 8 months, with effect from 24th February, 1934, or date of relief.

PROMOTIONS

Captains to be Majors

F. E. B. Manning. Dated 3rd October, 1933.

G. J. Smith. Dated 7th October, 1933.

Note.—(i) The promotion of Lieutenant-Colonel H. S. G. Haji, M.C., to the ranks of Major and Lieutenant-Colonel is antedated to 25th July, 1924, and 25th July, 1932, respectively.

(ii) The promotion of Major A. M. Ghosh to the rank of Major is antedated to 19th August, 1927.

Lieutenant to be Captain

Lieutenant (on probation) B. A. Porritt to be Captain (provisional), (on probation), 26th July, 1933.

The undermentioned Lieutenants (on probation) are granted antedates of seniority to 1st August, 1932:—

F. V. Stoneham.

J. M. Matthew.

F. I. Ashton.

I. Feinholz.

RETIREMENTS

Major-General W. C. H. Forster, C.I.E., V.H.S., with effect from the 19th July, 1933.

Lieutenant-Colonel G. E. Malcolmson, with effect from the 30th September, 1933.

Captain J. Acheson, on account of ill-health, with effect from the 1st August, 1933.

Notes

PEDIATRICIANS AND COW AND GATE MILK FOOD

At the close of the International Paediatric Congress held in London and opened by the Duke of York on 19th July, a number of the delegates accepted the invitation of Messrs. Cow and Gate, Ltd., to inspect their processes and methods at their West Country factories.

The party which numbered over 80, and included specialists in infants' diseases from fifteen different countries, was conveyed by express train specially chartered for the occasion to Wincanton in Somerset, the nearest of the zone of the company's factories in the famous pasture lands of the West.

On arrival the delegates were divided into parties and toured the works under experienced guides, aided by interpreters. Great keenness and interest was displayed throughout by the visitors, particularly as the much discussed question of safe milk supplies for children had been the subject of one of the principal papers at the Congress, and had given rise to a lengthy debate. It was generally agreed that Messrs. Cow and Gate had solved the question not only from the hygienic, but also from a nutritive point of view and American doctors present, accustomed to a high standard of milk production in their own country, declared they had never seen such immaculate methods and precision.

The delegates were shown the astounding aggregation of mucus, pus and infective microbial matter extracted at the factories from high grade, strained and apparently 'pure milk' before the actual processing took

place. Recollecting that raw milk of this description would be freely sold to the public, for infant feeding purposes, the exhibition was fittingly described by the guests as 'hair-raising'.

Some of the special foods prepared by the company were also on exhibition, such as Allergilac, for the treatment of allergic conditions in infancy. This food had been particularly referred to by Dr. Bray and other paediatricians at the Congress in the symposium on allergy.

At the end of the inspection the delegates sampled the crisp and creamy product which had been processed throughout to completion for their benefit and an adjournment was made for lunch to the White Horse Inn, a famous old hostelry of hunting renown.

After lunch the delegates drove by motor coach to Somerton factory in the vicinity of Glastonbury and enjoyed the delightful drive through the charming Blackmore Vale with its reminiscences of Thomas Hardy and of William Barnes, the Dorsetshire dialect poet.

SURGEONS GLOVES

We received a few pairs of their 'special process' surgeons gloves from the Leyland and Birmingham Rubber Co. (India), Ltd., with a request to give an opinion on their quality. They were handed to one of the leading surgeons of Calcutta who has informed us that these gloves are equal to any that he has ever used.

The address of the company is 12, Mission Row, Calcutta.

ADEXOLIN LIQUID

This preparation contains vitamins A and D in the proportions natural to high grade cod-liver oil, but at twenty times the concentration. Its potency is specially designed to secure flexibility in dosage—namely, to facilitate the administration of the smallest prophylactic or the largest therapeutic dose; and being practically tasteless and odourless it can be administered without risk of producing nausea. This preparation is valuable not only for all the purposes to which cod-liver oil prophylaxis and therapy have been applied, but like the capsules can be used for massive vitamin therapy as well. It is specially recommended for incorporation in the bottle feeds of infants.

THE TREATMENT OF TUBERCULOSIS WITH SANTUBEN

We have received a report from Dr. Eckstein at the Sanitarium Tatra Matliary in which he describes the use of this form of tuberculin in all forms of tuberculosis, and his summary is as follows:—

In the santuben treatment we have a very useful and absolutely harmless tuberculin specific. It is indicated in all cases where a specific irritance therapy is employed. Its influence on the general state of health, on the temperature and on the quantity of sputum was in most of the cases quite obvious. In no cases could a reaction to the nidus, or a general reaction be observed. The influence on the resorption of the serous discharges was also very evident, and discharges were quickly made to disappear.

DIGOXIN

In recent years it has been recognized that the leaves of *Digitalis lanata* have a much greater cardiotonic action than those of *Digitalis purpurea*, the species commonly used in medicine. Chemical investigations carried out in the experimental laboratories of the Wellcome chemical works resulted in the discovery and isolation of a new crystalline glucoside, which has been named digoxin. After pharmacological examination at the Wellcome physiological research laboratories the glucoside was submitted to the Therapeutic Trials Committee of the Medical Research Council, London, for clinical investigation. The results of this trial have recently been published. They indicate that digoxin is a useful member of the digitalis series, being particularly valuable in the treatment of auricular fibrillation when rapid effects are desired. Digoxin is rapid in its action even when given orally, so that intravenous injection is unnecessary save in exceptional cases. As a pure substance with well-defined chemical and physical properties digoxin provides a digitalis preparation of constant activity requiring no biological standardization. It has now been made available to the medical profession by Messrs. Burroughs Wellcome & Co., in whose laboratories it was discovered. The following products are issued, for oral administration: 'Tabloid' Digoxin 0.25 mgm. (bottles of 25 and 100) and Solution of Digoxin 0.5 mgm. in 1 c.cm. (bottles of 30 c.cm. and 250 c.cm.); for intravenous administration: 'Hypoloid' Digoxin 0.5 mgm. in 1 c.cm. (boxes of 10).

LACTOGEN

A SUBSTITUTE FOR MOTHERS' MILK

LACTOGEN is fresh cow's milk, modified and dried by a process embodying the latest scientific improvements, behind which stands the reputation of the Nestlé Company, as manufacturers of milk products for more than fifty years.

The chief chemical and physical properties of lactogen may be summarized as follows:

(1) When properly dissolved in water its composition very closely resembles the composition of human

(2) Every precaution is taken so as to enforce a strictly uniform composition of the manufactured lactogen.

(3) Extensive clinical tests prove that the digestibility of lactogen is materially in excess of that of best cow's milk.

In cow's milk, the fat exists in comparatively large globules. The modified fresh cow's milk, just before it is dried up into lactogen is forced under considerable pressure through minute openings which break up the fat globules into particles about ten times smaller in diameter; thereby the surface of the fat globules is enormously increased and the digestibility of the fat is increased in proportion.

Furthermore, experience teaches that whereas the curds formed by fresh cow's milk are thick and tough, the curds formed by lactogen are finely divided, exactly as is the case for human milk. These qualities obviously enhance the digestibility of lactogen.

(4) Extensive tests have been carried out in Nestlé's laboratories in regard to the vitamin contents of lactogen and a large number of biological experiments have proved that vitamins A, B and D are contained in this product. As far as vitamin C is concerned, it is directed that orange juice, which contains the anti-scorbutic vitamin in quantity, should be given daily to the baby, in order to guard against any possible deficiency in vitamin C in the milk.

This addition of fruit juice supplies a safety factor and is just as essential when an infant is fed with cow's milk or even at the breast.

(5) Bacteriological examinations are constantly carried out on the contents of the tin as packed for the market, and the results indicate the presence of not more than 500 colonies per gramme on an average. In addition, the pasteurization process has removed the danger of pathogenic organisms.

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